JPRS 76415

12 September 1980

USSR Report

SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 14, No. 4, 1980

FBIS FOREIGN BROADCAST INFORMATION SERVICE

NOTE

JPRS publications contain information primarily from foreign newspapers, periodicals and books, but also from news agency transmissions and broadcasts. Materials from foreign-language sources are translated; those from English-language sources are transcribed or reprinted, with the original phrasing and other characteristics retained.

Headlines, editorial reports, and material enclosed in brackets [] are supplied by JPRS. Processing indicators such as [Text] or [Excerpt] in the first line of each item, or following the last line of a brief, indicate how the original information was processed. Where no processing indicator is given, the information was summarized or extracted.

Unfamiliar names rendered phonetically or transliterated are enclosed in parentheses. Words or names preceded by a question mark and enclosed in parentheses were not clear in the original but have been supplied as appropriate in context. Other unattributed parenthetical notes within the body of an item originate with the source. Times within items are as given by source.

The contents of this publication in no way represent the policies, views or attitudes of the U.S. Government.

PROCUREMENT OF PUBLICATIONS

JPRS publications may be ordered from the National Technical Information Service (NTIS), Springfield, Virginia 22161. In ordering, it is recommended that the JPRS number, title, date and author, if applicable, of publication be cited.

Current JPRS publications are announced in Government Reports Announcements issued semimonthly by the NTIS, and are listed in the Monthly Catalog of U.S. Government Publications issued by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Indexes to this report (by keyword, author, personal names, title and series) are available through Bell & Howell, Old Mansfield Road, Wooster, Ohio, 44691.

Correspondence pertaining to matters other than procurement may be addressed to Joint Publications Research Service, 1000 North Glebe Road, Arlington, Virginia 22201.

JPRS 76415

12 September 1980

USSR REPORT

SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 14, No. 4, 1980

Translation of the Russian-language bimonthly journal KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA published in Moscow by the Meditsina Izdatel'stvo.

CONTENTS

PUBLICATION DATA

English title	:	SPACE BIOLOGY AND AEROSPACE MEDICINE, Vol 14, No 4, 1980
Russian title	:	KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, Vol 14, No 4, 1980
Editor	:	O. G. Gazenko
Publishing house	:	Meditsina
Place of publication	:	Moscow
Date of publication	:	July-August 1980
Signed to press	:	11 June 1980
Copies	:	1754

SURVEYS

UDC: 629.78.048.3/.4:612.233-087.4

HYGIENE AND TOXICOLOGY OF HUMAN WASTE GASES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1980 pp 3-7

[Article by V. V. Kustov and L. A. Tiunov, submitted 6 Jul 79]

[English abstract from source]

The review surveys the data published in the literature concerning involvement of human wastes in the formation of an artificial atmosphere of small enclosures designed for various purposes. The paper emphasizes applicability of theoretical data on human wastes to the solution of theoretical and practical problems of aerospace, marine, communal hygiene and clinical medicine as well as of biochemistry, physiology and other disciplines.

[Text] Exploration of space in manned spacecraft and development of resources of the oceans with the use of submarines and underwater laboratories have raised a number of complex medico-engineering problems related to production of life support equipment that would enable man to work in small sealed spaces for long periods of time. A special place is occupied by the problem of removing numerous chemicals from the artificial atmosphere of such habitats, particularly removal of waste gases.

Precise information about the composition, quantity and kinetics of discharge of such waste into the atmosphere, as well as determination of safe levels thereof in air, are required for development of special equipment for the above-mentioned purposes. Such information is not contained in the works of researchers who expounded the teaching on so-called anthropotoxins.

For this reason, scientists have concentrated for the last 20 years on identifying the composition of human waste in gas form with the use of modern methods of analytical chemistry (gas chromatography, infrared spectrophotometry and others) and determination of quantitative characteristics of waste, on the one hand, and evaluation of the toxic properties of such products, on the other, in order to set hygienic standards for levels thereof in the artificial atmosphere of small sealed compartments. The results obtained essentially revived the half-forgotten teaching on "anthropotoxins," and made it possible to assess from a contemporary vantage

point the significance of waste gases in forming the artificial atmosphere of manned spacecraft and the air environment of rooms with inadequate ventilation. The results of all these studies have been summarized and analyzed in a number of surveys [1, 2] and monographs [3].

In subsequent years, the results of research on hygiene and toxicology of human waste products were enriched with data pertaining to their involvement in forming the artificial atmosphere of submarines [4, 5].

The presence of such products in the space underneath clothing prompted work on a number of medico-engineering problems related to development of insulating protective gear and sanitary and toxicological evaluation thereof [6-9].

There was broad development of research on the effects of certain physical and chemical environmental factors on the intensity of production and elimination of gaseous metabolic products. It was established that elimination thereof increases substantially under the influence of moderate hypoxia [10], normobaric hyperoxia [11], with prolonged restriction of movement of animals [12] and man [13], and particularly under the combined effect of the last two factors [14].

A change in kinetics of discharge of certain gaseous metabolic products into the environment was demonstrated with exposure of man to high ambient temperature and during performance of physical work varying in intensity [15-18], as well as with exposure to x-rays [19, 20] and accelerations [21].

In addition to those listed above, studies using simulators were pursued with the involvement of human subjects. As a result of these studies, it was demonstrated that, in addition to gaseous metabolic products, there is also accumulation of other gaseous chemical compounds--human waste--in the artificial environment of sealed compartments, which are formed as a result of complex physicochemical conversions and bacterial decomposition of numerous organic substances contained in excrements, perspiration, sebum and urine [22, 23].

At the present time, data pertaining to overall output of human waste are used extensively in communal hygiene for determination of optimum air exchange in residential and public buildings [24], as well as for evaluation of the role of the latter in environmental pollution [25, 26]. The foregoing stresses the need to conduct further research in order to solve the theoretical and practical problems confronting aerospace, marine and communal hygiene, as well as other medical disciplines.

However, it is not only in the direction of defining the chemical composition of human waste and quantitative characteristics thereof that the main work in the field of hygiene must be pursued. It is also necessary to examine the distinctions of the combined effect of constituents in a mixture of human waste products with one another and with altered environmental

factors, which would permit more specific determination of previously proposed safe levels of metabolic products in the artificial atmosphere of airtight compartments and in the air environment of rooms with inadequate ventilation. Work in this direction is already in progress [7, 27, 28].

Studies dealing with demonstration of the effects of various chemical compounds (the presence of which cannot be ruled out in the artificial atmosphere of sealed compartments) on endogenous production and elimination of carbon dioxide and other metabolic products are also promising. It was found that these processes increase substantially under the influence of dihalo methanes (dichloromethane, dibromomethane, diiodomethane, bromochloromethane), which are metabolized in the body to carbon dioxide [29]. Tribromomethane, bromodichloromethane, halogen derivatives of the ethane (1,1-dichloroethane; 1,1,1-trichloroethane; 1,1,2-trichloroethane, halothane) and ethylene series (trichloroethylene and tetrachloroethylene), as well as oxygen-containing compounds of the methane series (formaldehyde, methanol, ethanol, formic acid, ethyl orthoformate and ethyl chloroformate) [30], have an analogous effect on this process. However, there may also be a genuine increase in endogenous production of carbon dioxide due to the effects, first of all, of toxic substances with hemolytic properties. For example, it was demonstrated that administration to rats of methylethylketone peroxide, which elicits development of hemolysis, is associated with intensification of elimination of endogenous carbon dioxide from the organism [31].

There must be further development of studies of the mechanism of formation of metabolic products for the purpose of selective control of intensity of their elimination. This direction of research has more than only applied significance. For example, the study of the mechanisms of endogenous formation of carbon dioxide served as an impetus for comprehensive research on processes of oxidative catabolism of porphyrin structures, which made it possible, for the first time, to assess the biological role of endogenous carbon dioxide not only and not so much as the end product of metabolism, but as a most important regulator of rate of degradation of hemoglobin and other porphyrin compounds [31-36]. In this regard, work directed toward determination of correlations between the level of production of endogenous carbon dioxide and biochemical structures related to the process of degradation of hemoglobin are of some interest. In particular, it was established that production of endogenous carbon dioxide is closely correlated with the level of unconjugated serum bilirubin and free iron of blood [37], activity of catalase and glucose-6-phosphate dehydrogenase of blood, hemolytic stability of erythrocytes and amount thereof in peripheral blood [31].

Studies of the mechanism of endogenous production of carbon dioxide and its interaction with cytochrome P-450 pave the way for analysis of the effect of this toxic substance on metabolism of exogenous compounds [38]. It was shown that cytochrome P-450, being the terminal oxidase of the extramitochondrial route of electron transport, controls the rate of function of

microsomal enzymes that are responsible for the metabolism of a number of drugs and industrial toxic agents.

With respect to research on the mechanism of endogenous production of acetone, a comprehensive study was made of the key enzyme of ketogenesis, acetyl coenzyme A thiolase. This enzyme catalyzes the reaction of condensation of acetyl CoA to acetoacetyl CoA. It was isolated from liver mitochondria in two isoforms [39]. It was also learned that not only the reaction of interaction of acetoacetyl CoA with another molecule of acetyl CoA, but interaction of this compound with succinyl CoA were sources of acetoacetate, the immediate precursor of acetone. This reaction is catalyzed by mitochondrial CoA transferase [40]. Acetoacetyl CoA is also condensed with a molecule of acetyl CoA, with production of β-hydroxy-β-methylglutaryl CoA. This compound is submitted to enzymatic degradation to acetoacetic acid and acetyl CoA. Acetoacetic acid is partially reduced enzymatically to β-hydroxybutyric acid through the action of NAD-dependent β-hydrobutyrate dehydrogenase and, in part, is submitted to spontaneous decarboxylation with production of acetone. All this indicates that more precise determination of the stages of endogenous production of acetone (like that of carbon dioxide and other metabolic products) points to the specific routes for goal-directed control of this process.

Finally, studies of the possibility of using data on elimination of endogenous products in exhaled air (as well as overall elimination thereof) as an integral criterion of the state of metabolic processes for the diagnosis and prognosis of a number of pathological states [41-43], and opinions concerning the effect of altered environmental factors on metabolism [41, 44] for the purpose of setting hygienic standards for safe levels thereof merit attention. In this regard, the research of American authors is of considerable interest [45-48]: they developed a special multistep cryogenic system for collecting samples of exhaled air and assaying various organic compounds in air. In these studies, the authors stress the importance of studying metabolic products in gas form for evaluation of the functional state of the corresponding biochemical systems. This refers, first of all, to assaying acetone, carbon dioxide, acetaldehyde, methylethyl ketone and isoprene.

Acetaldehyde is formed upon catabolism of the essential amino acid, l-threonine. Methylethyl ketone and methylisobutyl ketone are formed upon catabolism of fatty acids. Secretion of isoprene is related to metabolism of steroid structures, and it may characterize stress [47].

We should discuss one more question of theoretical importance. We believe it is wrong to consider the products of vital functions of man solely as "waste," "anthropotoxins" or "metabolic poisons." These substances play a certain biological role and perform physiological functions. For example, it has been established that fixation of carbon dioxide--a typical representative of the end metabolic gaseous products--is not only a property of plants and autotrophic microorganisms, but animals.

Stimulation of carbon dioxide uptake by animals intensifies their biosynthetic processes [49]. Carbon dioxide, along with ammonia, is used in synthesis of carbomoyl phosphate, which is essential to the production of pyrimidine bases and pyrimidine nucleotides. It has been demonstrated that there is a close link between reactions of carbon dioxide fixation and biosynthesis of lipids, carbohydrates, proteins, nucleic acids and nucleotides [49].

In addition to its involvement in synthesis of carbomoyl phosphate, ammonia is necessary for the production of glutamic acid. It participates in various amination reactions.

Acetone is carboxylated to acetoacetic acid and through it is included in metabolism of tricarboxylic fragments. At the same time, acetoacetic acid along with β-hydroxybutyric acid plays a substantial role in maintaining energy homeostasis [50]. We have already mentioned the role of endogenous carbon dioxide in regulation of the rate of oxidative degradation of heme.

Thus, it may be concluded that development of the teaching on products of vital functions has aided and is aiding in the solution of a number of practical problems of aerospace medicine. Studies of this problem enrich a number of theoretical disciplines with new scientific facts which, in turn, open up new ways for solving the practical problems put to biology and medicine.

BIBLIOGRAPHY

1. Kustov, V. V., and Tiunov, L. A. in "Farmakologiya. Khimioterapevticheskiye sredstva. Toksikologiya" [Pharmacology. Chemotherapeutic Agents. Toxicology], 1969, "Problems of Toxicology," Moscow, 1971, pp 8-28.

2. Sedov, A. V. TEOR. I PRAKT. FIZ. KUL'TURY [Theory and Practice of Physical Culture], No 7, 1974, pp 68-70.

3. Kustov, V. V., and Tiunov, L. A. "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 11, 1969.

4. Gulyar, S. A.; Shaparenko, B. A.; Kiklevich, Yu. N.; et al. "The Human Body and the Underwater Environment," Kiev, 1977.

5. Rodkey, F. L.; Umstead, M. E.; Engel, R. R.; et al. AEROSPACE MED., Vol 45, 1974, pp 397-400.

6. Gorodinskiy, S. M.; Bavro, G. V.; Kuznets, Ye. I.; et al. GIG. I SAN. [Hygiene and Sanitation], No 1, 1973, pp 45-49.

7. Sedov, A. V.; Surovtsev, N. A.; Mazneva, G. Ye.; et al. in "Mediko-tekhnicheskiye problemy individual'noy zashchity cheloveka" [Medico-Engineering Problems of Personnel Protection], edited by M. I. Vakar, Moscow, Vyp 15, 1974, pp 66-69.

8. Koshcheyev, V. S.; Salivon, S. G.; and Bogachuk, G. P. GIG. I SAN., No 1, 1977, pp 56-60.

9. Koshcheyev, V. S.; Sedov, A. V.; and Bogachuk, G. P. Ibid, No 3, 1979, pp 28-31.

10. Kolosova, T. S., and Tiunov, L. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1973, pp 17-21.

11. Kustov, V. V.; Abidin, B. I.; Belkin, V. I.; et al. Ibid, No 5, 1972, pp 3-5.

12. Kustov, V. V.; Belkin, V. I.; Abidin, B. I.; et al. Ibid, No 2, 1971, pp 14-17.

13. Sokolov, N. L.; Nefedov, Yu. G.; Savina, V. P.; et al. Ibid, No 1, pp 57-59.

14. Kustov, V. V.; Abidin, B. I.; Belkin, V. I.; et al. Ibid, No 1, 1976, pp 66-68.

15. Gorodinskiy, S. M.; Sedov, A. V.; Mazon, A. N.; et al. Ibid, No 2, 1970, pp 78-80.

16. Idem, Ibid, No 5, 1971, pp 62-68.

17. Sedov, A. V.; Mazon, A. N.; Gaziyev, G. A.; et al. in "Mediko-tekhnicheskiye problemy individual'noy zashchity cheloveka," edited by S. M. Gorodinskiy, Moscow, Vyp 3, 1969, pp 13-21.

18. Sedov, A. V.; Zhukova, L. I.; and Mazneva, G. A. GIG. TRUDA [Industrial Hygiene], No 9, 1971, pp 36-38.

19. Kolosova, T. S.; Tiunov, L. V.; Kustov, V. V.; et al. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 4, 1970, pp 613-617.

20. Tiunov, L. A.; Zherbin, Ye. A.; and Zherdin, B. N. "Radiation and Toxic Agents," Moscow, 1977.

21. Coltman, C. A.; Dudley, G. M.; and Leverett, S. AEROSPACE MED., Vol 40, 1969, pp 627-630.

22. Matsumoto, K. E., and Partridge, D. H. J. CHROMATOGR. SCI., Vol 85, 1973, pp 31-34.

23. Pliskovskaya G. N.; Savina, V. P.; Il'in, Ye. A.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 1, 1975, pp 31-33.

24. Gubernskiy, Yu. D.; Dmitriyev, M. T.; D'yachkova, N. G.; et al. GIG. I SAN., No 7, 1976, pp 26-29.

25. Sidorenko, G. I.; Gubernskiy, Yu. D.; Dmitriyev, M. T.; et al. in "Gigiyenicheskiye aspekty okhrany okruzhayushchey sredy" [Hygienic Aspects of Environmental Protection], Moscow, Vyp 4, 1976, pp 116-119.

26. Sidorenko, G. I.; Gubernskiy, Yu. D.; and Dmitriyev, M. T. GIG. I SAN. No 5, 1978, pp 10-15.

27. Abidin, B. I.; Belkin, V. I.; Kustov, V. V.; et al. KOSMICHESKAYA BIOL., No 6, 1978, pp 63-67.

28. Abidin, B. I.; Kustov, V. V.; Belkin, V. I.; et al. Ibid, No 5, 1979, pp 44-48.

29. Kubic, V. L.; Anders, M. W.; Engel, R. R.; et al. DRUG METAB. DISPOSIT. BIOL. FATE CHEM., Vol 2, 1974, pp 53-57.

30. Fodor, G. G., et al. JBER. MED. INST. LUFTHYG. SILIKOSEFORSCH., No 6, 1973, pp 98-105.

31. Kliorin, A. I., and Tiunov, L. A. "Functional Dissimilarity of Erythrocytes," Leningrad, 1974.

32. Drabkin, D. L. ANN. N.Y. ACAD. SCI., Vol 174, 1970, pp 49-63.

33. Tenhunen, R.; Marver, H. S.; and Schmid, R. J. LAB. CLIN. MED., Vol 75, 1970, pp 410-421.

34. O'Carra, P., and Colleran, E. BIOCHEM. J., Vol 125, 1971, p 110.

35. Tenhunen, R.; Marver, H.; Frager, W.; et al. BIOCHEMISTRY, Vol 11, 1972, pp 1716-1720.

36. Tenhunen, R. ANN. CLIN. RES., Vol 8, Suppl 17, 1976, pp 2-19.

37. Linch, S., and Moedo, A. J. LAB. CLIN. MED., Vol 79, 1972, pp 85-87.

38. Montgomery, M., and Rubin, K. J. APPL. PHYSIOL., Vol 35, 1973, pp 601-607.

39. Huth, W.; Dierich, C.; von Oenhausen, V.; et al. BIOCHEM. BIOPHYS. RES. COMMUN., Vol 56, 1974, pp 1069-1077.

40. Deana, R.; Meneghello, R.; Manzi, L.; et al. BIOCHEM. J., Vol 138, 1974, pp 481-486.

41. Nikberg, I. I.; Murashko, V. A.; and Leonenko, I. N. VRACH. DELO [Medical Record], No 12, 1972, pp 112-114.

42. Kuznetsova, T. I.; Savina, V. P.; Ryzhkova, V. Ye.; et al. in "Aviakosmicheskaya meditsina," Moscow--Kaluga, Pt 2, 1979, pp 92-93.

43. Bensinger, T. A.; Brouillard, R. P.; and Conrad, M. E. BRIT. J. HAEMAT., Vol 29, 1975, pp 487-494.

44. Krotoszynski, B.; Gabriel, G.; and O'Neill, H. J. CHROMATOGR. SCI., Vol 15, 1977, pp 239-244.

45. Concle, J.; Adams, S.; and Mabson, W. AEROSPACE MED., Vol 38, 1967, pp 491-499.

46. Idem, Ibid, Vol 41, 1970, pp 1051-1058.

47. Concle, J.; Camp, B.; and Welch, B. ARCH. ENVIRONM. HLTH., Vol 30, 1975, pp 290-295.

48. Liebich, H. M.; Bertsch, W.; Zlatkins, A.; et al. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 1002-1007.

49. Gulyy, M. F. "The Nature and Biological Significance of Some Adaptive Metabolic Reactions of Organisms," Kiev, 1977.

50. Newsholme, E., and Start, K. "Regulation of Metabolism," Moscow, 1977.

EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 629.78:[612.17+612.2

CARDIORESPIRATORY SYSTEM REACTIONS OF COSMONAUTS TO EXERCISE FOLLOWING LONG-TERM MISSIONS ABOARD THE SALYUT-6 ORBITAL STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 8-11

[Article by A. V. Beregovkin, A. S. Vodolazov, V. S. Georgiyevskiy, L. I. Kakurin, V. V. Kalinichenko, N. V. Korelin, V. M. Mikhaylov and V. V. Shchigolev, submitted 7 Aug 79]

[English abstract from source]

The cosmonauts who made 96- and 140-day missions aboard the Salyut-6 orbital station showed no disorders in cardiovascular function or regulation during graded exercises. They displayed certain changes that could be attributed to deconditioning upon return to 1 g. These findings give evidence that efficient cardiovascular prophylaxis to exercises in prolonged space flight is possible.

[Text] This study [1-4] deals with analysis of changes in cardiorespiratory system reactions to graded physical loads following 96- and 140-day flights aboard the Salyut-6 orbital station.

Methods

A bicycle ergometer was used for the physical load test. An increasing graded load was used, with mandatory inclusion of the level of 600 kg-m/min. The parameters used to assess the state of the cardiorespiratory system were recorded and estimated in the same manner as in our previous studies [3].

Results and Discussion

First expedition: The commander (CDR-1) and flight engineer (FE-1) tolerated a two-step load (600 kg-m/min × 3 min + 750 kg-m/min × 3 min) well in the preflight period. The reaction of their cardiorespiratory system to this load was the same as in other cosmonauts prior to missions [1-4].

On the 5th postlanding day, both cosmonauts exercised for 3 min, the load constituting 300 kg-m/min, in the nature of a preliminary test, during

which we recorded only arterial pressure (AP) and the EKG. Tests involving 3-min exercise constituting 600 kg-m/min were performed on the 6th day by FE-1 and 7th day by CDR-1, during which we recorded the entire set of parameters of the cardiorespiratory system. On the 12th day, another test was performed by both crew members: two-step load (600 kg-m/min × 3 min + 750 kg-m/min × 3 min) for CDR-1 and three-step load for FE-1 (300 kg-m/min min × 3 min + 600 kg-m/min × 3 min + 750 kg-m/min × 1 min).

Exercise on the bicycle ergometer after landing was not associated with any functional disturbances. At the same time, there was some worsening of regulation of the cardiovascular system and endurance of the physical load. Thus, the cosmonauts subjectively perceived a load of 300 kg-m/min in the same way as 750 kg-m/min before the flight. The Table lists the main parameters of circulation and respiration in the 3d min of exercise constituting 600 kg-m/min.

Some parameters of the cardiorespiratory system in the 3d min of exercise constituting 600 kg-m/min 1 month before and 1 week after flight aboard Salyut-6 orbital station

Parameter	Time of examination	96-Day flight				140-Day flight			
		CDR-1		FE-1		CDR-2		FE-2	
		BG*	load	BG	load	BG	load	BG	load
HR, per min	Before flight	75	114	56	109	64	105	58	103
	After "	80	119	66	119	82	118	96	120
Ejection period, ms	Before "	253	220	283	235	261	230	271	220
	After "	240	200	255	170	250	207	245	170
Systolic AP, mm Hg	Before "	140	170	135	140	115	160	110	160
	After "	140	180	120	165	130	160	130	180
Diastolic AP, mm Hg	Before "	70	95	75	90	70	90	60	75
	After "	75	90	80	80	85	95	70	90
Cardiac load index, arbitrary units	Before "	105	194	76	153	74	156	64	165
	After "	112	214	79	196	107	189	112	216
Oxygen uptake, ml/min	Before "	254	1206	238	1445	297	1350	313	1221
	After "	264	1209	254	1335	296	1349	313	1320
Oxygen pulse, ml/beat	Before "	3.4	10.6	4.1	13.3	4.6	12.8	5.4	11.9
	After "	3.3	10.2	3.8	11.2	3.6	11.4	3.6	11.0
Cardiac index, ml/min/m²	Before "	2740	7790	2930	8760	—	—	—	—
	After "	2630	7540	2560	8090	—	—	—	—

*Background

First of all, it should be noted that there was an increase in intensity of cardiac function during exercise in both cosmonauts. The heart rate (HR) increased and end systolic AP rose. Their product, the so-called cardiac load index [5] rose by 10%, as compared to preflight data, in CDR-1 and by 28% in FE-1, which was indicative of an increase in energy expended by the heart for the same amount of exercise. Intensification of cardiac function resulted in a circulatory minute volume and oxygen uptake close

to the preflight levels only in CDR-1. In FE-1, these parameters were 8 and 11% lower, respectively, than the preflight levels.

The intensity of cardiac function and, apparently, excessive sympathetic stimulation were also manifested by shortening of the ejection period, as compared to the proper time for a given HR, by 11% for CDR-1 and 28% for FE-1. There was a decrease in efficiency of cardiac function with regard to oxygen transport. Thus, oxygen [respiratory?] pulse decreased by 4% in CDR-1 and by 16% in FE-1, as compared to preflight levels.

In assessing the reactions of the cosmonauts' cardiorespiratory system to physical exercise, we can note increased intensity of its function and uneconomical function. However, such an increase in intensity provided for an adequate supply of oxygen to the body only for CDR-1, whereas it was diminished in FE-1, and this apparently reflected worsening of myocardial contractility.

Second expedition: The commander (CDR-2) and flight engineer (FE-2) participated in a 140-day mission. Like the crew of the first expedition, they tolerated well the test on the bicycle ergometer prior to the flight. The recorded parameters were consistent with the reactions of a healthy person.

The test on the bicycle ergometer was conducted on the 7th postflight day. Two grades of exercise were required, in accordance with the physical condition of the cosmonauts: 450 kg-m/min × 3 min + 600 kg-m/min × 3 min. Neither crew member experienced any unpleasant sensations while pedaling. The CDR-2 observed that he could have performed the same amount of exercise on the 1st postflight day.

We were impressed by the increased intensity of cardiac function, even at rest in the initial position. There was substantial increase in HR and AP. The cardiac load index was 44% higher than the preflight level for CDR-2 and 75% higher for FE-2. The uneconomical function of the cardiorespiratory system was reflected in the 22% decrease of oxygen pulse in CDR-2 and 34% decrease in FE-2, as compared to preflight levels.

Taking into consideration the baseline, the reaction to the physical load conformed with its size. Thus, there was a 20% increase in cardiac load index of CDR-2 and 31% increase in that of FE-2, as compared to preflight values. But this increase was less marked than in the initial position at rest.

Cardiac function was more intensive in FE-2. It was manifested by an 18% shorter ejection period than the proper time for a given HR. At the same time oxygen uptake was even 11% greater than before the flight. In CDR-2, the ejection period was consistent with the proper value, and oxygen uptake was at the preflight level. Oxygen pulse of CDR-2 decreased by 11% and that of FE-2 decreased by 8%, in accordance with increase in HR, as compared to preflight levels, which reflected less economical cardiac function.

After 7 weeks of readaptation, which was concluded in a sanatorium, both cosmonauts had no difficulty in performing three-step exercises (450 kg-m/min × 3 min + 600 kg-m/min × 3 min + 750 kg-m/min × 3 min). Their reactions to the physical load were entirely restored to preflight levels.

The feature in common in changes in reactions of the cardiorespiratory system of all four cosmonauts was their transient, functional nature and complete recovery in the readaptation period. None presented disturbances of cardiac rhythm or signs of myocardial ischemia. At the same time, there were some differences between reactions, which could have been related to the distinctions of the mission and measures used to prevent deconditioning.

It can be seen that, with increase in duration of the flight, there was an increase in intensity of cardiorespiratory functions. Thus, the differences in HR, as compared to preflight levels, were as follows: +5/min for CDR-1, +10 for FE-1, +13 for CDR-2 and +17 for FE-2. The fact that an increased intensity of cardiac function was noted mainly at rest among the crew of the second expedition merits attention. Thus, there was a 44% increase in cardiac load index of CDR-2 and 75% increase in FE-2, whereas among crew members of the first expedition this indicator at rest was close to preflight levels. Consequently, the increased intensity of cardiac function was referable primarily to a change in regulation at rest and could not be interpreted as a sign of poorer contractility of the heart. We had observed similar changes previously in individuals who had spent a long time on bed rest [6].

According to most parameters, the reactions of the cardiorespiratory system were quite similar in CDR-1, CDR-2 and FE-2, and they could be classified in the same category of states. This state can be described as a manifestation of deconditioning at earth's gravity and alteration of regulation. Only FE-1 presented signs of physical deconditioning, which consisted of decreased circulatory minute volume and oxygen uptake. If we were to relate the above-mentioned differences to the accounts of the cosmonauts as to the volume of preventive exercises performed during the flight, this state can be considered close to the individual optimum for CDR-1, CDR-2 and FE-2. The preventive set of exercises was apparently inadequate only for FE-1. On the whole, there is every reason to believe that the system used for the prevention of deconditioning did adequately preserve cardiorespiratory tolerance of physical loads. The reactions of crew members involved in the expeditions aboard the Salyut-6 orbital station to exercise did not differ from those of the crew of the Salyut-4 orbital station, who were involved in a 63-day mission. This enables us to evaluate more accurately the results of physical load tests conducted after prior flights. Evidently, it was not so much the incompleteness of adaptation reactions during the 30-day mission, as previously assumed [7], as the improvement of preventive measures during each of the subsequent, longer expeditions that was the cause of less beneficial reactions after the 30-day flight, as compared to the 63-day one.

Thus, the results of these studies are indicative of the possibility of effective prev ntion of deconditioning of the cardiorespiratory system with reference to physical loads during long-term space flights. At the same time, the increased intensity of cardiac function with increase in duration of flights is indicative of a need to refine methods of preventive exercises in order to protect regulatory mechanisms against overloads. Apparently, such refinement of the methods of exercise, as well as regular performance thereof, would make it possible to conduct even longer space missions.

BIBLIOGRAPHY

1. Mikhaylov, V. M.; Georgiyevskiy, V. S.: Smyshlyayeva, V. V.; et al. KOSMICHESKIYE ISSLED. [Space Research], No 5, 1972, pp 778-782.

2. Beregovkin, A. V.; Baburina, Ye. B.; Georgiyevskiy, V. S.; et al. in "Gagarinskiye chteniya. 4-ye. Sektsiya 'Problemy aviakosmicheskoy meditsiny i biologii.' Materialy" [4th Gagarin Lecture. Section on "Problems of Aerospace Medicine and Biology." Proceedings], Moscow, 1974, pp 40-46.

3. Beregovkin, A. V.; Vodolazov, A. S.; Georgiyevskiy, V. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1976, pp 24-29.

4. Kakurin, L. I.; Katkovskiy, B. S.; Mikhaylov, V. M.; et al. in "Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniya" [Space Flights Aboard the Soyuz Series Craft. Biomedical Studies], Moscow, 1976, pp 230-265.

5. Shkhvatsabaya, I. K.; Aronov, D. M.; and Zaytsev, V. P. "Rehabilitation of Patients With Cardiac Ischemia," Moscow, 1978.

6. Georgiyevskiy, V. S. in "Fiziologicheskiye problemy detrenirovannosti" [Physiological Problems of Deconditioning], edited by A. V. Korobkov, Moscow, 1970, pp 58-70.

7. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. KOSMICHESKAYA BIOL., No 5, 1976, pp 3-18.

UDC: 629.78:612-087.5:616-001.12-031.22-092.6

REACTIONS TO LBNP TEST OF THE CREW OF THE SALYUT-5 ORBITAL STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 11-16

[Article by V. A. Degtyarev, V. G. Doroshev, Z. A. Kirillova, N. A. Lapshina, S. I. Ponomarev and V. N. Ragozin, submitted 19 Jan 79]

[English abstract from source]

During the 49-day mission (first expedition) the Commander did not show a decline in LBNP tolerance, whereas the Flight-Engineer showed a progressive decrease in LBNP tolerance beginning with Mission Day 23. During the 17-day mission (second expedition) the Flight-Engineer exhibited greater cardiovascular reactions to LBNP than the Commander. Postflight examinations confirmed the observations made in the weightless state.

[Text] During the mission aboard the Salyut-5 orbital station, much attention was devoted to indirect evaluation and prediction of orthostatic stability of crew members. For this purpose, the functional test with LBNP [lower body negative pressure] was used [1-5]. We submit below the principal results of LBNP tests in the preflight period, during and after the flight. These data broaden existing conceptions of the distinctions of cosmonaut adaptation to weightlessness.

Methods

The test was conducted with the cosmonauts immersed in a vacuum tank to the level of the superior crests of the iliac bones. Rarefaction of -30-40 mm Hg was created in the first 15-20 s to measure blood pressure in the jugular vein. After this, pressure was raised to -25 mm Hg for 2 min, then dropped to -35 mm Hg for 3 min. The subjects were in horizontal position during LBNP in the preflight and postflight periods. Polynome-2M equipment was used to record the tachooscillogram of the brachial artery, kinetocardiogram of the region of the apex beat, arteriovenous pulsogram of cervical vessels and sphygmogram of the femoral artery.

RESULTS AND DISCUSSION

In the preflight period, the commander of the first expedition (CDR-1) presented best endurance of LBNP tests and orthostatic stability, while the flight engineer of the first expedition (FE-1) presented the poorest. The crew of the second expedition, CDR-2 and FE-2, occupied an intermediate position with regard to orthostatic stability and LBNP tolerance; however, the reaction to LBNP was somewhat better in FE-2. A total of 9 tests with LBNP were conducted in weightlessness, including 3 for CDR-1, 4 for FE-1, 1 each for CDR-2 and FE-2.

As can be seen in Figure 1, the most moderate and stable reactions to LBNP were found in CDR-1. In spite of the heavy work load and fatigue, his orthostatic stability diminished negligibly in weightlessness. Of the three tests conducted in weightlessness, maximum changes were observed with LBNP on the 45th day of the flight, when maximum increment of heart rate (HR) constituted 22%, while the decline of stroke (SV) and minute (MV) blood volumes constituted 39 and 25%, respectively. In the preflight period, the greatest changes in cardiovascular parameters were noted in the LBNP test performed 5 days before the flight. HR increment constituted 13%, while SV and MV decreased by 49 and 42%, respectively. The unusual reaction to LBNP on the 6th day (increase in SV and MV in the 1st min to 25 mm Hg) was apparently a residual effect of raising pressure in the tank [compartment] following the somewhat extended effect of rarefaction (-40 mm Hg) created at the start of the test to measure venous pressure. The results of in-flight tests were consistent with the postflight findings. Orthostatic stability and endurance of LBNP test were quite satisfactory in CDR-1 after landing.

In FE-1, the hemodynamic changes under the influence of LBNP in weightlessness were more marked, as they were on earth (Figure 2). Already in the first test conducted on the 7th day of the flight, the increment of HR constituted 53%, and maximum decline of SV and MV constituted 67 and 50%, respectively. The rate of propagation of the pulse wave over the aorta increased by 56%. Pulse pressure dropped by 31%. There was a decrease in endurance of LBNP starting on the 23d day. In spite of the fact that the increase in HR remained approximately the same, it reached progressively higher values in view of the higher base level prior to the test, and it did not stabilize at the levels attained. These changes in the reaction were interpreted as a sign of diminished orthostatic stability. The LBNP tests on the 30th and 44th days of the flight were stopped by the physician of the mission control center 30-60 s before the scheduled time. On the 30th day of the flight, there was a drastic decrease in amplitude of pulse curves and dicrotic wave of the sphygmogram to the isoline at the start of the 2d min of rarefaction to -35 mm Hg. As a rule, such changes in sphygmograms accompany severe hemodynamic disturbances, and they are one of the most reliable signs of development of a presyncopic state [6]. The FE-1 did not observe any worsening of his condition; however, he evidently made several subconscious movements in the vacuum tank, as if stepping from one

foot to the other. Involvement of the muscle pump immediately improved venous return, and there was relative compensation of the cosmonaut's condition.

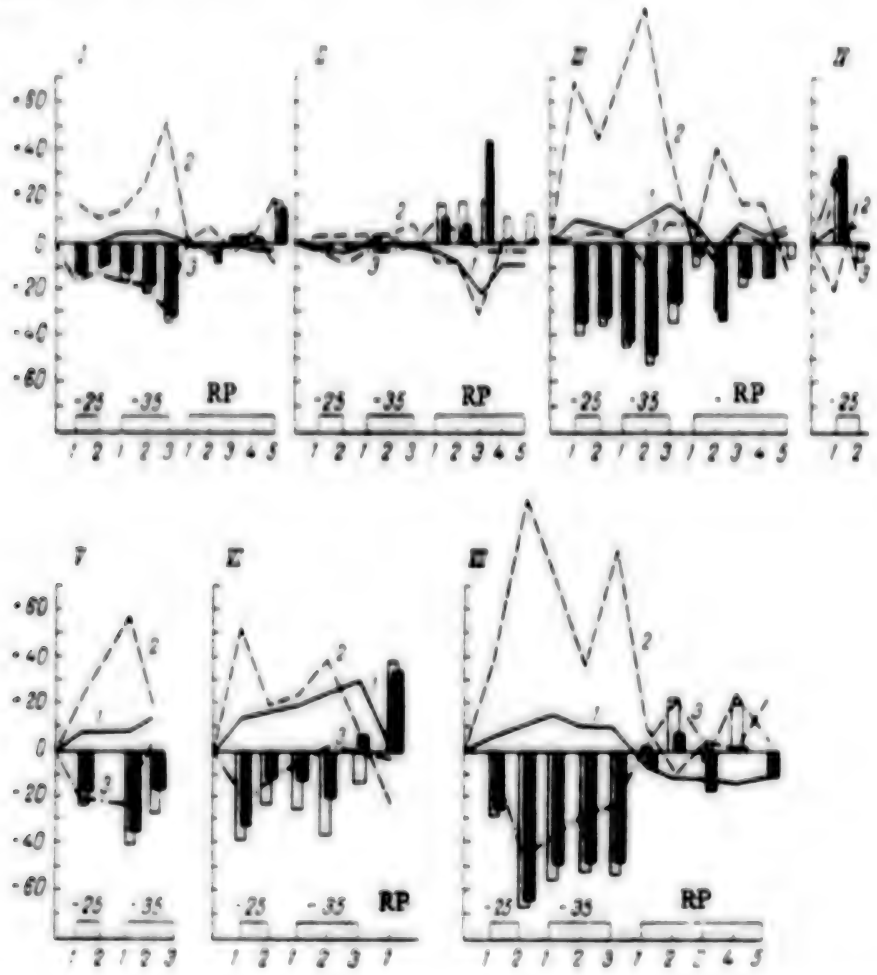


Figure 1. Changes in hemodynamic parameters of CDR-1 during LBNP

Here and in Figures 2-4:

1) heart rate
2) actual specific resistance
3) pulse pressure

White columns: SV

Black columns: MV

I-III) 6 mos 19 days, 78 days and 5 days before flight

X-axis: rarefaction (mm Hg) and duration (min) of LBNP; y-axis, deviation from base level (%)

RP) recovery period

IV-VI) 6th, 14th and 45th days of flight

VII) 4th postflight day

As we know [7], at least 10% of the LBNP tests performed in weightlessness ended with a presyncopic state in American astronauts. As a rule, they occurred with rarefaction of -50 mm Hg. The reaction of FE-1 described above was the first instance of worsening of a cosmonaut's condition during

an LBNP conducted in weightlessness with rarefaction of -35 mm Hg. If we were to compare the dynamics of circulatory parameters of FE-1 in the course of this in-flight test and prior preflight tests, we would see that he also presented considerable hemodynamic changes with analogous levels of rarefaction 14 months prior to the flight. However, these changes were not associated with development of a presyncopic state or, perhaps, signs thereof were missed by the physicians. This preflight test was characterized by a significant decrease in arteriolar tonus in the initial state. Actual peripheral resistance was 22% less than it should have been, while minimum, mean and lateral arterial pressure were the lowest of all levels ever recorded for FE-1.

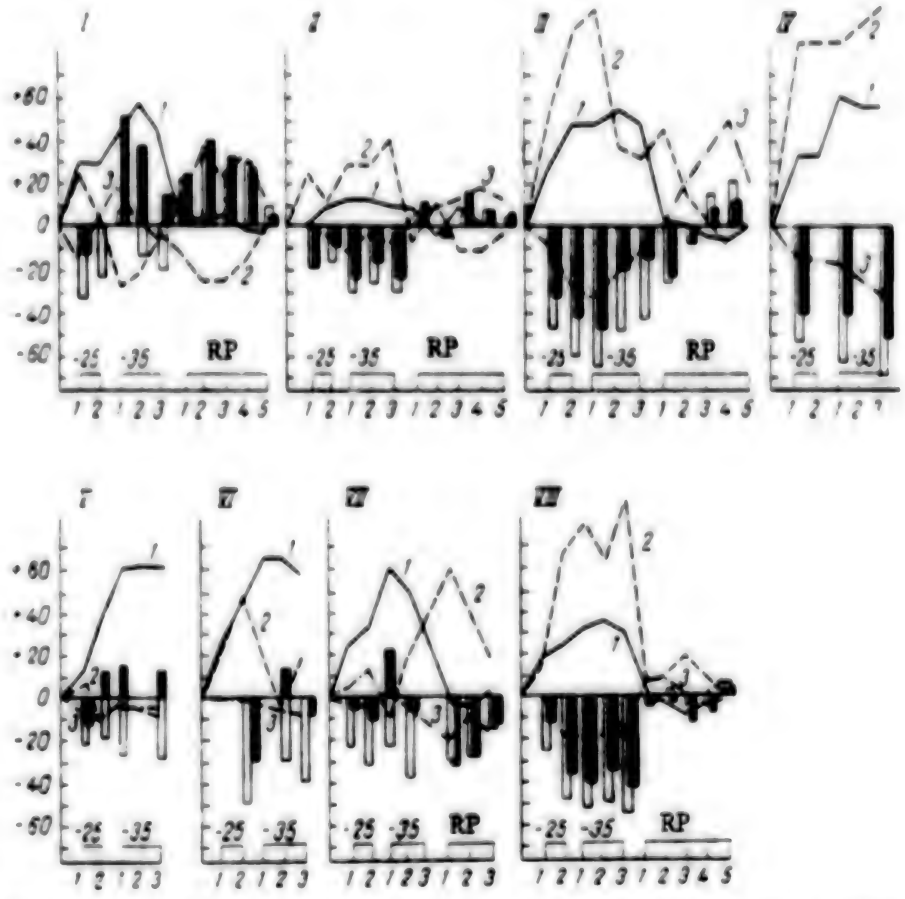


Figure 2. Changes in hemodynamic parameters of FE-1 during LBNP

I-III) 1 year 42 days, 78 days and 5 days before flight
IV-VII) 7th, 23d, 30th and 44th flight days
VIII) 4th postflight day

FE-1 failed to present such drastic changes in arteriolar tonus prior to the LBNP test in weightlessness; however, when tested on the 40th day of the flight under basal metabolic conditions, they were recorded. On that day,

the actual peripheral resistance was 15% less than it should be, while minimum pressure was the lowest for the entire flight period (42 mm Hg). Thus, lability of vascular tonus, which had not been evaluated in the preflight period, could have been the immediate cause of progressively worsening endurance of LBNP and orthostatic stability in weightlessness for FE-1. As was to be expected, FE-1 presented diminished postflight orthostatic stability.

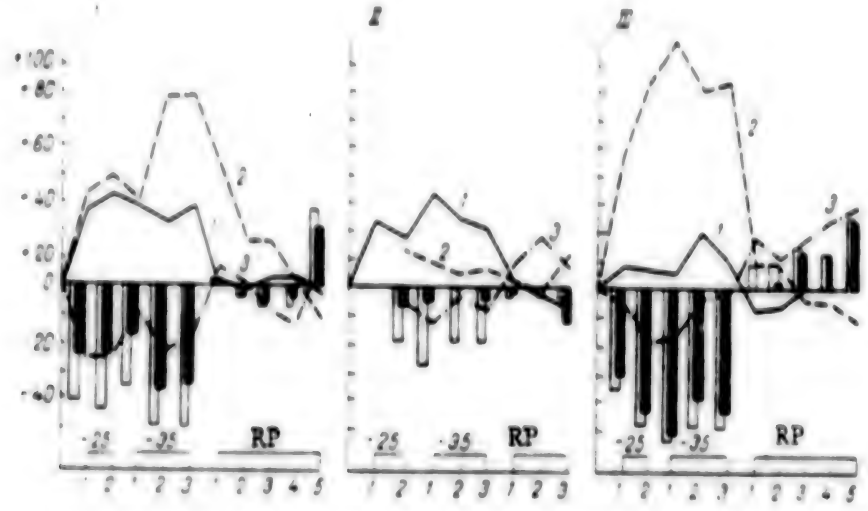


Figure 3. Changes in hemodynamic parameters of CDR-2 during LBNP

I) 6 months before flight II) 13th flight day III) 4th postflight day

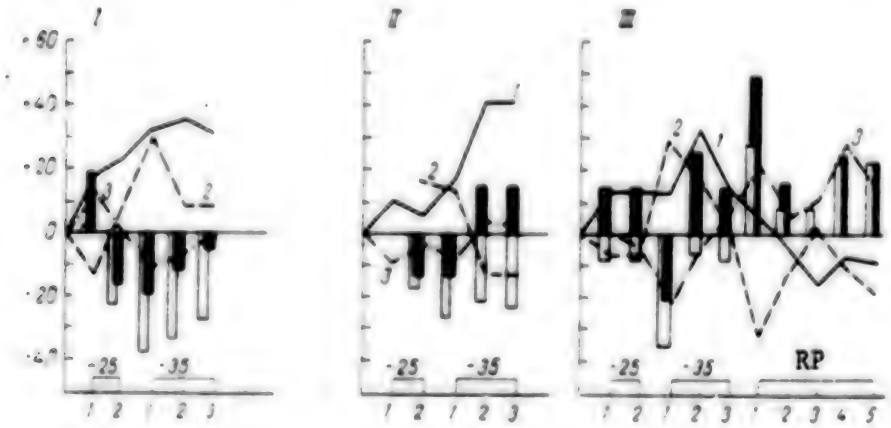


Figure 4. Changes in hemodynamic parameters of FE-2 during LBNP

I) 1 year 10 days before flight II) 12th flight day III) 4th postflight day

The CDR-2 submitted to the LBNP test once (13th day) during the 17-day period of weightlessness. The reaction of his cardiovascular system was moderate (Figure 3). Maximum changes in most hemodynamic parameters were less marked than before the flight.

In FE-2, the LBNP test performed on the 12th flight day was associated with more marked changes in hemodynamic parameters than in CDR-2. By the end of the test, his HR increased by 46%, while MV increased by 14% (Figure 4), which was indicative of poorer tolerance of the test. The results of postflight examination of the second crew confirmed the findings in weightlessness. During the readaptation period, orthostatic stability was better in CDR-2 than FE-2.

Thus, the functional LBNP test conducted during the mission aboard the Salyut-5 orbital station made it possible to predict rather reliably the orthostatic stability of the cosmonauts. There was retention of individual distinctions of the subjects' reactions in weightlessness. The poorer tolerance of LBNP and orthostatic stability of FE-1 was attributable to lability of tonus of resistive vessels.

BIBLIOGRAPHY

1. Degtyarev, V. A.; Popov, I. I.; and Kalmykova, N. D. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 132-157.

2. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1974, pp 47-52.

3. Degtyarev, V. A.; Doroshev, V. G.; Batenchuk-Tusko, T. V.; et al. Ibid, No 3, 1977, pp 26-31.

4. Berry, Ch. A. in "Man in Space," Moscow, 1974, pp 51-75.

5. Lamb, L. S., and Stevens, P. M. AEROSPACE MED., Vol 36, 1965, pp 1145-1151.

6. Kukushkin, Yu. A. in "Fizicheskiye metody i voprosy metrologii biomeditsinskikh izmereniy" [Physical Methods and Problems of Metrology of Biomedical Measurements], Moscow, 1976, pp 174-176.

7. Hoffler, G. W.; Wolthis, R. A.; and Johnson, R. L. AEROSPACE MED., Vol 45, 1974, pp 807-820.

UDC: 629.78:616.981.25-008.97-078

PREFLIGHT DISTINCTIONS OF STAPHYLOCOCCUS AUREUS CARRIERS AMONG COSMONAUTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 16-20

[Article by R. Yu. Tashpulatov, T. N. Nikolayeva and Ye. V. Guseva,
submitted 9 Nov 78]

[English abstract from source]

A preflight study of Staphylococcus aureus carriage in cosmonauts has demonstrated that the microorganism harbors in 79.4 % of the tested and microbial foci of the carriers amount to 10^3 ml. The isolated Staphylococcus aureus strains show a pronounced plasma coagulatory, α-toxic activity and 67.4 % of them can be typed by the International set phages. Prophylactic administration of the native staphylococcal anatoxin increases specific antistaphylococcal immunity, reduces or eliminates completely Staphylococcus aureus in the upper respiratory airways.

[Text] The extreme factors of space flights, which elicit functional changes in man, may cause a change in nature and quantity of conditionally pathogenic microorganisms, in particular, Staphylococcus aureus.

The process of carrying S. aureus is the result of a complex set of biological phenomena attributable to immunobiological properties of the macroorganism, on the one hand--its local and general reactivity-- and nature of microbial flora of the surface of the mucosa of the upper respiratory tract (URT), as well as its biocenotic interactions with S. aureus, on the other [1-3].

The mucosa of the URT, mainly of the anterior segments of the nasal passages, is the principal habitat of staphylococci [4, 5].

At the present time, it has been demonstrated that exposure of the macroorganism to adverse factors (such as somatic disease, extensive and prolonged surgical intervention, prolonged hypokinesia) can cause formation of the carrier state and lead to an increase in S. aureus sites in the URT [6, 7].

Carriers of the "resident type" are of particular significance, and S. aureus is demonstrable in them constantly, in considerable quantities. The pathogenesis of the carrier state is based on inadequate local immunity of URT mucosa, related to impaired synthesis of secretory immunoglobulin A, shortage of serum immunoglobulin A and decline of lysozyme level in saliva [8, 9].

In this regard, the question arises of the desirability of detecting S. aureus carriers among cosmonauts preparing for long-term missions. It is imperative to implement microbiological testing of isolated S. aureus strains and develop measures for the prevention of diseases during long-term flights against the background of diminished immunological resistance.

The objectives of this study were as follows: quantitative analysis of S. aureus isolated from the cosmonauts' URT in the preflight period and qualitative evaluation of isolated strains of S. aureus.

Methods

The material to be examined was collected in the form of washings from the mouth, throat and nose, which were cultured, after dilution, on egg yolk and salt solution agar. After 48 h of incubation at 37°C, 3-4 lecithin-positive colonies of S. aureus were removed. The S. aureus strains were submitted to qualitative identification by means of demonstration of DNAase using acid precipitation in dishes, as well as hemolytic activity, plasma-coagulating activity and α-toxic activity. All of the isolated strains were typed with phages of the international set in a dosage of 100 TR [toxic reacting?]. A total of 34 subjects were screened (2-5 times), and 107 strains of S. aureus were studied.

The quantitative characteristics of S. aureus sites in carriers thereof and quantitative parameters of isolated strains were compared to those of essentially healthy individuals (control group).

Results and Discussion

Of the 34 individuals examined, 27 were carriers of S. aureus (79.4%) (Table 1). In three of them, S. was repeatedly isolated from the nose, mouth and throat simultaneously in amounts of 10^2-10^3 over the period of the study (April 1976 to November 1977). It must be noted that all of the isolated strains of staphylococci were of the same phagotype: 54/83A, 6/42E/47/53/54/75/83A and 53/75/77 in one case, 53/83A in another and 29/52A/79 in a third.

As can be seen in Table 1, 29.6% of the carriers had S. aureus only in the nasal cavity, and the mean size of bacterial foci constituted $1.4 \cdot 10^2$; in 37.1% of the carriers, the biotope of staphylococci were the mouth and throat, the focus of which was $2.7 \cdot 10^2$ in size, and in 33.3% of the 27 carriers, S. aureus was isolated simultaneously from the nose, mouth and throat. The density of the microorganisms constituted $6.8 \cdot 10^2$ in the nose,

$3.3 \cdot 10^2$ in the mouth and throat. Thus, the quantitative assay of S. aureus among cosmonauts who were carriers thereof virtually failed to differ from the findings in the control group ($P > 0.05$; see Table 1).

Table 1. Data pertaining to S. aureus carriers among individuals in the control group and cosmonauts prior to flights

Topographic regions examined	Control group				Cosmonauts			
	number of carriers	%	bact. focus		number of carriers	%	bact. focus	
			log	absolute number			log	abs. number
Nasal cavity	10	32.3	3.2±0.38	$1.7 \cdot 10^3$	8	29.6	2.1±0.4	$1.1 \cdot 10^2$
Mouth and throat	9	29.0	2.2±0.21	$1.5 \cdot 10^2$	10	37.1	2.4±0.2	$2.7 \cdot 10^2$
Mouth and throat Nose	12	38.7	2.4±0.35	$2.3 \cdot 10^2$	9	33.3	2.5±0.26	$3.3 \cdot 10^2$
			2.9±0.46	$7.8 \cdot 10^2$			2.8±0.2	$6.5 \cdot 10^2$
Total carriers	31	60.8	—		27	79.4	—	
Total examined	51				34			

Note: log--geometric mean number of bacterial cells.

It should be noted that the size of the bacterial focus in each carrier and biological properties of S. aureus were rather constant over the long observation period.

The biological properties of isolated strains of S. aureus are listed in Table 2. Mean plasma-coagulation reaction time constituted 89.4±2.7 min, α-toxin titer was 1:165±18.6, and the above-mentioned indicators of pathogenisity were more marked than in strains of S. aureus isolated from individuals in the control group ($P_{pl} < 0.05$, $P_{\alpha\text{-toxin}} < 0.001$; see Table 2).

Table 2. Biological properties of strains of S. aureus isolated from the control group and cosmonauts

Group examined	Total stmins	Titer of α-toxin	Plasma-coagulating reaction time, min
Control (51 people)	110	1.89±8.47	154±29.79
Cosmonauts (34 people)	107	1.165±18.6	89.4±2.7
P		<0.001	<0.05

An important finding of this study was the phage group distribution of the isolated S. aureus strains. Table 3 shows that 67.4% of the analyzed strains could be typed with the international set of phages, and the phage characteristics were as follows: 18.7% of the isolated strains were referable to phage group I, 3.7% to group II, 29.9% to group III and 14.9% to the mixed group. Only 32.6% of the clones of S. aureus could not be typed with these phages (see Table 3). Phage group III strains and those that could not be typed with the international set of phages were predominant.

Table 3. Phage group distribution of isolated strains of S. aureus

Group of subjects	Phage groups											
	I		II		III		mixed		non-group		untyped	
	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
Control	13	11.8	18	16.4	15	13.6	10	9.1	1	0.9	53	48.2
Cosmonauts	20	18.7	4	3.7	32	29.9	16	14.9	—	—	35	32.6

As shown by previous studies [10], strains referable to the mixed phage group (2.5±0.427) and those that were not typed by phages of the international set (2.35±0.748) were the most virulent. The virulence levels of strains in phage groups I-III were about the same, constituting 1.74±0.318, 1.74±0.35 and 1.82±0.127, respectively. Consequently, we can state that there was prevalence of strains with higher virulence indexes.

The foregoing, as well as the results of previous studies, demonstrated the necessity of preventive measures against possible development of diseases of staphylococcal etiology in cosmonauts just prior to flights. We selected for this purpose the unadulterated staphylococcal anatoxin [toxoid] produced by the Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences.

Tests [11, 12] established that administration of this immunopreparation to resident carriers elicits a quantitative decrease (to the extent of elimination) of bacterial sites of S. aureus in the URT, selectively stimulates factors of specific α-antitoxic immunity (α-AT titer), nonspecific humoral and cellular immunity.

A course of preventive administration of native staphylococcal anatoxin to carriers of S. aureus, and mainly those of the "resident type," just prior to flights raised significantly the level of the specific α-AT titer (from 0.5 to 14.0 AU [antitoxic units]/ml) and had a stimulating effect on different parameters of local immunity, causing complete elimination of S. aureus phage type 29/52A/79 from the URT (from $5 \cdot 10^1$-$2 \cdot 10^1$ to 0).

After completion of a 96-day flight, the cosmonaut retained a high level of specific antistaphylococcal immunity, which persisted for the entire month of the postflight observation period (18.0 AU/mℓ on the 1st day, 16.0 on the 7th and 8.0 AU/mℓ on the 33d postflight day). No S. aureus was demonstrable.

Immunization of the spacecraft commander with native staphylococcal anatoxin raised the level of specific α-AT titer, causing gradual increase in amount of staphylococcal α-antitoxin in blood (1.0 AU/mℓ before immunization, 8.0 AU/mℓ before lift off and 24.0 AU/mℓ after the flight). A high level of staphylococcal α-antitoxin persisted in the cosmonaut's blood (22.0 AU/mℓ) 14 days after the flight. Against this background, $5 \cdot 10^1$ S. aureus phage type 3C, 52A/3C was isolated from the skin surface and $1 \cdot 10^4$, phage type 3C, from the nose on the 1st postflight day. On the 7th-14th postflight days, the "bacterial landscape" of the nose included isolated colonies of S. aureaus, phage type 3C, 3C/55/71/52/52A. In this case, we can assume that there was postflight exogenous infection of the nose and skin of this cosmonaut with S. aureus.

The change in level of staphylococcal α-antitoxin in blood occurred at a later time in the flight engineer than the commander, and it was less marked. The α-AT titer constituted 8.0 AU/mℓ on the 1st postflight day and 10.0 AU/mℓ on the 14th, S. aureus constituting 10^2, and it was not typed with the phages of the international set.

Thus, preflight immunization with native staphylococcal anatoxin provided stable and prolonged antistaphylococcal immunity, against the background of which S. aureus isolated from the cosmonauts' URT did not manifest its pathogenetic action. Immunization disinfected the carrier of S. aureus, phage group I (phage type 29/52A/79).

The results of this study revealed the following: the incidence of S. aureus carriers among the screened group of healthy individuals is rather high (79.4%); the size of the bacterial foci is of the order of 10^2; the isolated strains of S. aureus have marked plasma coagulating and α-toxic activity, and in 67.4% of the cases they can be typed with the phages in the international set; preventive administration of staphylococcal anatoxin leads to an increase in specific antistaphylococcal immunity, quantitative decrease in and total elimination of S. aureus from the URT of carriers of the "resident type."

BIBLIOGRAPHY

1. Zakaryan, L. M. in "Kurskiy med. in-t. Nauch. konf. 45-ya. Programmnyye materialy" [45th Scientific Conference of Kursk Medical Institute, Program Notes], Kursk, 1971, pp 277-280.

2. Tychinin, V. A. VRACH. DELO [Medical Record], No 6, 1973, pp 138-143.

3. Shenifield, H. R. in "Staphylococcal Infections," Basel, 1973, pp 541-547.

4. Favorova, L. A., and Mordvinova, N. B. ZH. MIKROBIOL. [Journal of Microbiology], No 9, 1974, pp 73-79.

5. Heszko, P. B., and Pryjma, J. in "Staphylococci and Staphylococcal Infections," Basel, 1973, pp 581-594.

6. Zaloguyev, S. N.; Shinkareva, M. M.; and Utkina, T. G. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1970, pp 54-59.

7. Ostroumov, P. B.; Chukhlovin, B. A.; Kushko, I. V.; et al. ZH. MIKROBIOL., No 5, 1973, pp 125-129.

8. Chukhlovin, B. A.; Ostroumov, P. B.; and Ivanova, S. P. KOSMICHESKAYA BIOL., No 6, 1971, pp 61-65.

9. Smirnova, A. M.; Troyashkin, A. A.; and Paderina, Ye. M. "Microbiology and Prevention of Staphylococcal Infections,: Leningrad, 1977, p 151.

10. Nikolayeva, T. N., and Tashpulatov, R. Yu. J. MIKROBIOL., No 12, 1976, pp 124-127.

11. Nikolayeva, T. N. "Occurrence of Postoperative Suppurative Infection of Staphylococcal Etiology in Surgical Patients," candidatorial dissertation, Moscow, 1977.

12. Lesnyak, A. T. "Effect of Surgical Intervention on Immunity and Microbial Flora of Surgical Patients," candidatorial dissertation, Moscow, 1978.

UDC: 612.014.477-064].017.2

STATIC ENDURANCE OF RATS AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 20-22.

[Article by A. R. Kotovskaya and A. A. Shipov, submitted 26 Feb 79]

[English abstract from source]

Static endurance of rats exposed to an 18.5-day flight aboard the biosatellite Cosmos-936 was measured. The recovery rate of static endurance of rats flown in an onboard centrifuge generating 1 g was similar to that of rats used as synchronous controls. It is concluded that artificial gravity helps to maintain cardiovascular, muscular and respiratory functions at an almost normal level.

[Text] It is known that adaptation to weightlessness is associated with a decrease in functional capabilities of the organism and its resistance to various factors, primarily those related to returning to earth's gravity [1-3].

Studies conducted aboard the Cosmos-782 biosatellite established that restoration of such an integral indicator of the condition of the organism as static endurance occurs more slowly in rats after a space flight than in animals used in a ground-based control experiment [4]. It was assumed that the use of artificial gravity [AG] of 1 G aboard Cosmos-936 would eliminate or attenuate the observed differences.

Methods

The criterion of static endurance of the animals was maximum time that they could hold on to a pole [5]. Since preliminary experiments established that "holding on" time was a function (Figure 1) of the animals' weight (normogram), we took the percentile of actual "holding on" time in relation to the time determined from the normogram was used as the indicator of static endurance.

We tested male Wistar-SPF rats, which were divided into the following groups: FW_3 group of animals submitted to weightlessness; FC_2 group submitted to AG

during 18.5-day space flight; SW_3 group of animals in the ground-based synchronous experiment, in which the habitat aboard the biosatellite and dynamic factors inherent in the launching, descent from orbit and landing phases were simulated; C_2^0--animals rotated on a short-arm ground-based centrifuge at the rate of 53.3±0.3 r/min, which equals the angular velocity of the onboard centrifuge (in order to test the effect of rotation factors on the parameters studied) and, finally, VC_3--vivarium control animals. The experimental conditions were described in detail previously [6].

The animals were examined 4 days before the flight, as well as on 0 day (day that the biosatellite landing), 3d, 6th, 16th and 24th days of the aftereffect period. The animals in ground-based control experiments were examined at the same times.

Results and Discussion

Throughout the observation period the static endurance of animals in the VC_3 group did not differ reliably from the levels on the normogram (i.e., close to 100%).

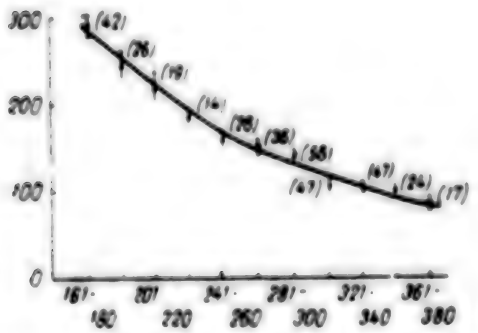


Figure 1.
Normogram of static endurance of Wistar-SPF rats
X-axis, weight (g); y-axis, "holding on" time
The numbers over the experimental points (in parentheses) indicate the number of animals tested

After the experiment, endurance of group SW_3 animals decreased by 45%, as compared to background value and the value inherent in group VC_3 (Figure 2a). Consequently, the prolonged stay in individual cages led to a significant decrease of static endurance. This decrease is probably related to the relative decrease in range of movements performed by the animals and, as a result, some degree of asthenization and deconditioning.

There was greater decrease in static endurance (by 65%) of animals in the FW_3 group 3 h after landing (0 day) than in the SW_3 group (see Figure 2a). An analogous correlation between static endurance of animals in groups SW_3 and FW_3 was noted at the first examination and in the experiment aboard Cosmos-782 (Figure 2b).

In subsequent tests, static endurance of animals in groups SW_3 and FW_3 increased drastically at first, then reverted more slowly to the base level. But while recovery occurred on the 6th-10th day in the SW_3 group, endurance

remained low up to the 24th day, and the differences from the 100% level were reliable on the 6th, 11th and 16th days. Similar patterns of restoration of static endurance had also been noted in the experiment aboard Cosmos-782 biosatellite (see Figure 2b).

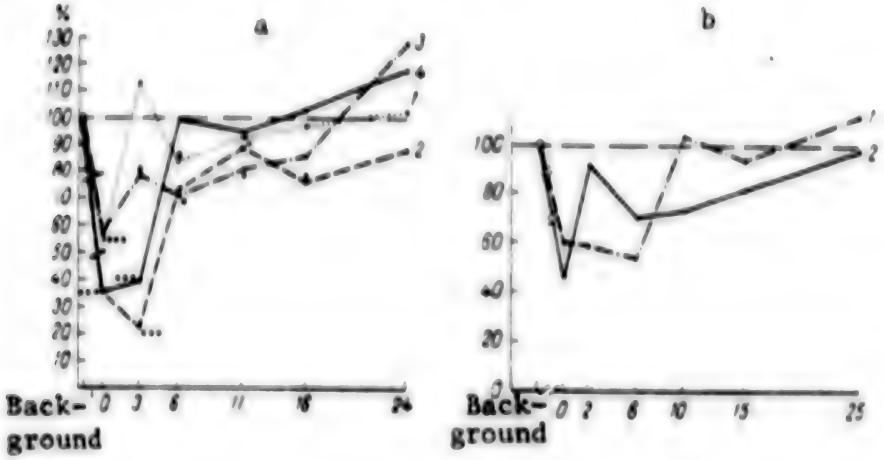


Figure 2. Static endurance of rats after flights aboard Cosmos-936 (a) and Cosmos-782 [4] (b) biosatellites

X-axis, day of examination; x-axis, static endurance (% of values determined on normogram). Asterisks refer to differences that are reliable in relation to the 100% level; 1-4--SW_3, FW_3, $C_2{}^0$ and FC_2 groups, respectively

Static endurance immediately after the flight was decreased in group FC_2 animals, just as it was in group FW_3 (see Figure 2a), i.e., it was lower than in group SW_3. The additional decrease in endurance of FC_2 animals, as compared to SW_3, could be induced by the adverse effect of precession and Coriolis accelerations. Indeed, animals kept in a rotating system for a long time develop a dynamic muscular stereotype of counteraction to forces that arise when moving in such systems [7]. Upon exiting from this system, the developed stereotype could impair for a time coordination of movements and natural distribution of tonus of different muscle groups and, consequently, make it difficult to hang on to the post. Diminished sensitivity of the functional system of the semicircular canals, observed in animals after a long stay in a rotating system, could also lead to an analogous effect [8]. However, the above arguments cannot be deemed convincing, since no additional decrease in endurance was noted in the $C_2{}^0$ group of animals exposed to the same magnitude of precession and Coriolis accelerations. Perhaps the decreased endurance of group FC_2 animals, as compared to group SW_3, is related to the fact that the animals in the onboard centrifuge were exposed to lower gravity because of the AG gradient in the floor-ceiling phase [segment] (1-0.7 G).

The absence of differences in static endurance at the first examination of animals kept for a long time under basically different conditions (weightlessness and AG in the flight experiment, stationary and rotating environment in the ground-based one) and appearance of distinct differences in the dynamics of recovery processes upon subsequent tests (see Figure 2a) indicate apparently that the stress reactions associated with the end of the experiment had some significance with regard to change in this parameter at the first examination.

The second and subsequent tests during the aftereffect period revealed higher endurance parameters in group FC_2 than FW_3 (see Figure 2a). Recovery of static endurance already occurred on the 6th post flight day. It should be stressed that the rate of recovery of static endurance was about the same in group FC_2 as in SW_3. Since static endurance is related to the function of many systems of the organism and, first of all, the cardiovascular, respiratory and muscular, we are justified in concluding that AG of 1 G is helpful in holding the function of these systems at about the normal level.

BIBLIOGRAPHY

1. Gazenko, O. G., and Gyurdzhian, A. A. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 6, 1967, pp 22-42.

2. Kotovskaya, A. R. "Human Endurance of Accelerations as Applied to Space Flights," author abstract of doctoral dissertation, Moscow, 1970.

3. Pestov, I. D., and Geratevol', Z. Dzh. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 1, 1975, pp 324-369.

4. Kotovskaya, A. R.; Shipov, A. A.; Ayzikov, G. S.; et al. in "Vliyaniye dinamicheskikh faktorov kosmicheskogo poleta na organizm zhivotnykh" [Effect on Animals of Dynamic Space Flight Factors], Moscow, 1979, pp 129-135.

5. Shipov, A. A., and Markin, A. S. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1977, pp 83-84.

6. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. Ibid, No 6, 1979, pp 18-22.

7. Matthews, B. H. C. J. PHYSIOL. (London), Vol 122, 1953, p 31P.

8. Shipov, A. A., and Ovechkin, V. G. KOSMICHESKAYA BIOL., No 2, 1980, pp 25-30.

UDC: 612.015.2.014.477

COMPARATIVE STUDY OF EFFECTS OF WEIGHTLESSNESS AND ARTIFICIAL GRAVITY ON DENSITY, ASH, CALCIUM AND PHOSPHORUS CONTENT OF CALCIFIED TISSUES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 23-26

[Article by A. A. Prokhonchukov, N. S. Komissarova, N. A. Zhizhina and A. I. Volozhin, submitted 10 Oct 78]

[English abstract from source]

The studies were carried out on 30 rats flown for about 10 days aboard the biosatellite Cosmos-936 (5 centrifuged rats including) and 25 ground-based control rats. Postflight the centrifuged rats did not show significant differences in the density, mineral saturation, distribution of vascular channels in bones, ash, calcium and phosphorus content in skeletal bones and teeth as compared with the parameters in synchronous and vivarium controls. In the weightless rats these values were significantly lowered.

[Text] The problem of disturbances in mineral metabolism in the course of prolonged space flights has still not been studied very much. At the same time, analysis of metabolic changes in cosmonauts who were involved in long space flights indicates that there are changes in mineral metabolism and loss of mineral salts from skeletal bones [1, 2]. Analogous changes were found in dogs after a 22-day flight aboard Cosmos-110 biosatellite [3], as well as monkeys after a 9-day flight aboard Biosatellite-III [4].

Disturbances referable to calcium and phosphorus metabolism, as well as decreased mineralization of bones and teeth of experimental animals whose movements were restricted, were demonstrated in ground-based tests using radioisotope, roentgenophotometric and other methods [5-9].

In this regard, the hypothesis was expounded that the increased elimination of calcium during space flights is attributable to weightlessness along with hypokinesia [10]. For this reason, the experiment aboard the Cosmos-936 satellite with artificial gravity [11] is of great interest.

Methods

The following groups of rats (total of 55 animals) were studied: FW_1--animals taken on a space flight under weightless conditions; FC_1--animals exposed to artificial gravity during space flight; SW_1 and SC_1--corresponding groups of animals in ground-based synchronous experiments, SC^0_1--animals rotated on short-arm centrifuge and VC_1--animals in the vivarium control sacrificed immediately after the experiment, as well as FW_3, FC_2, SW_3, SC^0_2 and VC_3--which are analogous groups (with the exception of SW_2) of animals sacrificed 25 days after the experiment [11].

The physical properties of bone tissue were examined: density, mineral content, distribution of vascular canals [9], ash content, calcium and phosphorus content of bones and teeth [10].

The following skeletal tissues were examined: vertebra, rib, scapula, femur (epiphysis and diaphysis), humerus (epiphysis and diaphysis), maxilla and mandible, and teeth (molars and incisors), to a total of 605 samples of calcified tissues with three-fold analysis of each specimen. The experiments were programmed (determination was made of optimum size of sampling of animals and specimens); the results were submitted to statistical processing according to Student.

Results and Discussion

The density of bone per unit volume of femoral diaphysis and mineralization were 44.4% lower in the SW_1 group of rats ($P<0.01$) than in VC_1. Analogous changes in physical properties of bone tissue were noted in the SC_1 group. A 26.7% decrease ($P<0.05$) in mineralization of osseous tissue was found in group FC_1. A 26.6% increase in density of osseous tissue was demonstrated in the FC_2 group, which is apparently related to increased mineralization thereof. No differences between groups were demonstrable 25 days after the experiment, with regard to density and mineralization.

Morphological studies revealed that there was a relative decrease in number of smallest vascular canals (5 arbitrary units) due to increase in number of large canals in rats used in the ground-based experiments with exposure to different factors. There was more than two-fold increase in number of canals 11-15 arbitrary units in size in the femoral diaphysis of rats in groups SW_1 and FC_1, as compared to VC_1.

After the space flight, rats in group FW_1 presented an increase in number of large canals, as compared to control animals. There was also appearance of canals 40 arbitrary units in size [area], which did not occur in the synchronous experiment (SW_1). Use of the centrifuge during the space flight (FC_1) did not prevent the increase in number of large canals in the femoral diaphysis of experimental rats.

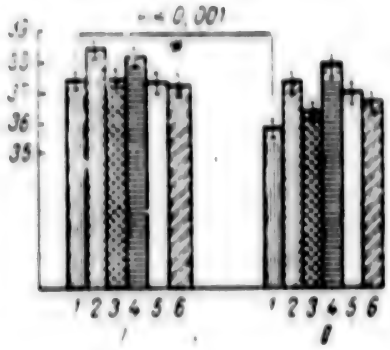


Figure 1.
Calcium content of humeral epiphysis (I) and diaphysis (II) 6 h after landing. Asterisk marks reliable difference (P<0.001) between epiphysis and diaphysis indices for animals in the FW1 group
1) FW_1 3) SW_1 5) VC_1
2) FC_1 4) SC_1 6) SC_1^0

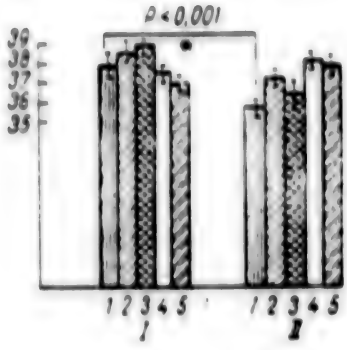


Figure 2.
Calcium content of humeral epiphysis (I) and diaphysis (II) 25 days after landing. Asterisk marks reliable difference (P<0.001) between epiphysis and diaphysis indices for the FW3 group
1) FW_3 3) SW_3 5) SC_2^0
2) FC_2 4) VC_3

There was an increase in number of canals with an area of 5 arbitrary units 25 days after the space flight (FW_3), as compared to SW_3 and VC_3 groups. This trend was the opposite of the one demonstrated immediately after the space flight.

There was a 1-5% decrease in ash content of all skeletal bones and teeth examined after the space flight (FW_1), as compared to groups SW_1 and VC_1; a reliable (P<0.05) 3-5% decrease was demonstrated only in teeth and the mandible. There was a reliable (P<0.001) change in ash index (by 10-11%) in the diaphysis of the humerus and femur, as compared to epiphysis.

A reliable (P<0.05) increase (by 3-5%) in ash index was observed after 25 days of readaptation in all examined tissues of animals in the FW_3 group, with approximation of control group levels. This index remained virtually unchanged in the teeth and skeletal bones of FC_2 animals, it increased (by 2-5%) reliably (P<0.05) in the SW_3 group, whereas it was essentially the same in VC_3 as in VC_1. There was a reliable (P<0.01) 4-6% elevation of this index in long bones; it remained reliably (P<0.001) diminished (by 10%) in the diaphyses, as compared to epiphyses.

There was a reliable (P<0.05) decrease (by 2-11%) in calcium content of skeletal bones and teeth of FW_1 animals, as compared to VC_1, and this was also demonstrable in the synchronous control. In the vivarium control (VC_1), this index was close to the level in the FC_1 group. In all groups of animals, there was a reliable (P<0.001) increase (by 6-9%) in calcium content of femoral and humeral epiphyses, as compared to diaphyses (Figure 1).

There was a reliable ($P<0.05$) increase in stable calcium content of molars (by 6%) 25 days after the experiment in group FW_3, as compared to FW_1. In FC_2, the identical findings were made. Animals in group SW_3 presented a tendency toward normalization of calcium content of all tissues examined, as compared to groups VC_3 and SW_1. The same reliable ($P<0.01$) difference (by 6-9%) between levels for the epiphysis and diaphysis was observed in long bones as was found immediately after landing (Figure 2).

There was a reliable 16-18% decrease in phosphorus content of all tissues examined in FW_1 animals, as compared to VC_1, and 6-10% decrease as compared to SW_1 animals. A negligible (2-4%) but reliable ($P<0.05$) decrease was noted in the molars and other tissues examined, as compared to the figures for the synchronous (SW_1) and vivarium (VC_1) controls. There was a reliable ($P<0.001$) decrease (by 20%) in phosphorus content of the femoral and humeral diaphyses, as compared to the epiphyses of the same bones. There was redistribution of this parameter in both groups (SW_1 and SC_1) in the synchronous experiment. The phenomenon of redistribution of parameters for the diaphysis and epiphysis was not demonstrated in the vivarium control (VC_1).

There was a reliable ($P<0.05$) increase (by 6%) in phosphorus content of molar ash in animals of the FW_3 group, as compared to the FW_1 group. This parameter was identical in the FC_3 group to the one for the vivarium control (VC_3). In other tissues, phosphorus content did not differ from levels in the vivarium control. In the vivarium control, the levels in all tissues were the same in the first and second examination.

Thus, after the flight, there were no appreciable differences in density, mineralization, distribution of vascular canals in bone, ash index, stable calcium and phosphorus content of skeletal bones and teeth of animals submitted to centrifugation, as compared to the levels in the synchronous experiment and vivarium control. The parameters were significantly lower in animals that were not put on the centrifuge.

The findings on mineral metabolism in bones and teeth are consistent, to some extent, with the results of prior studies aboard Cosmos-605, Cosmos-690 and Cosmos-782 biosatellites [12], since the data on redistribution of parameters for epiphyses and diaphyses of long bones, found in the studies of material from Cosmos-782, were confirmed by the findings from examining material from Cosmos-936.

BIBLIOGRAPHY

1. Biryukov, Ye. N., and Krasnykh, I. G. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1970, pp 42-46.

2. Grandpierre, R. REV. MED. AERONAUT., Vol 10, 1971, pp 135-141.

3. Biryukov, Ye. N. "Change in Mineralization of Osseous Tissue and Calcium Balance Associated With Experimental Hypokinesia and Space Flights," candidatorial dissertation, Moscow, 1968.

4. Mack, R. B. AEROSPACE MED., Vol 42, 1971, pp 828-833.

5. Lobachik, V. I., and Yegorov, B. B. in "Eksperimental'nyye issledovaniya gipokinezii, izmenennoy gazovoy sredy, uskoreniy, peregruzok i drugikh faktorov" [Experimental Studies of Hypokinesia, Altered Gas Environment, Accelerations, G Forces and Other Factors], Moscow, 1968, pp 15-17.

6. Yegorov, B. B.; Lobachik, V. I.; and Kleymenova, L. N. KOSMICHESKAYA BIOL., No 1, 1969, pp 55-58.

7. Prokhonchukov, A. A.; Kovalenko, Ye. A.; Kolesnik, A. G.; et al. STOMATOLOGIYA [Stomatology], No 4, 1970, pp 1-6.

8. Pavlova, M. N.; Volozhin, A. I.; and Muradova, I. Sh. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 8, 1975, pp 35-38.

9. Volozhin, A.I. "Pathogenesis of Impaired Calcium Metabolism in Mineralized Tissues During Long-Term Hypokinesia," author abstract of doctoral dissertation, Moscow, 1977.

10. Prokhonchukov, A. A.; Tigranyan, R. A.; Kolesnik, A. G.; et al. KOSMICHESKAYA BIOL., No 1, 1977, pp 26-30.

11. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. Ibid, No 6, 1970, pp 18-22.

12. Prokhonchukov, A. A.; Kolesnik, A. G.; Komissarova, N. A.; et al. STOMATOLOGIYA, No 3, 1978, pp 23-25.

UDC: 612.465-06:629.78

MORPHOLOGICAL STUDY OF RAT KIDNEYS AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 26-31

[Article by A. S. Pankova, submitted 20 Aug 78]

[English abstract from source]

Kidneys of SPF Wistar rats flown for 18.5 days aboard the biosatellite Cosmos-936 and sacrificed 4.5-13 hours or 25 days postflight were taken under morphological study. An exposure of rats to artificial gravity inflight brought about a smaller increase in the kidney mass and a better readaptation of animals on return to 1 g. It is suggested that blood redistribution in the kidneys due to renal circulation shunting and, possibly, fluid transfer from the vascular bed to interstitial space are the factors causing an increase in kidney mass. No differences in the kidneys of weightless and centrifuged rats were found.

[Text] Changes in fluid-electrolyte metabolism are among the dominant forms of hemodynamic disorders observed in cosmonauts on the 1st day after returning to earth. Numerous studies of renal function of cosmonauts have been conducted both after brief flights and after prolonged weightlessness [1, 2]. It was established that with the transition from weightlessness to earth's gravity there is a decrease in diuresis and excretion of electrolytes, and increase in antidiuretic activity of blood [3-5].

An analogous reaction was demonstrated in rats flown aboard Cosmos-605 and Cosmos-782 biosatellites, which presented diminished elimination of fluid and electrolytes on the 1st day after returning to earth [6, 7]. Morphological examination of the kidneys of these rats revealed an increase in activity of the juxtaglomerular system (JGS) of the kidneys and increase in their weight [8]. The latter finding remained unexplained, since no pathological changes that could be the cause of weight gain were demonstrable in either the renal parenchyma or interstitium.

Methods

SPF Wistar rats (Institute of Endocrinology, Czech Academy of Sciences) were divided into five groups. The first consisted of animals flown aboard Cosmos-936 for 18.5 days and sacrificed immediately (within 4.5-13 h) or 25 days after landing; the second consisted of rats rotated during the flight on a centrifuge with exposure to artificial gravity (AG) of 1 G; the third and fourth groups were rats in the ground-based synchronous experiment (control for weightless and control for centrifuge, respectively), and the fifth group consisted of rats in the vivarium control. The experimental conditions were described in detail elsewhere [9].

The animals in the second to fifth groups were sacrificed at the same times as the first group. In all experimental animals, we weighed the kidneys and submitted them to histological examination. The kidneys were fixed in 10% formalin or Zenker's formol solution, then embedded in paraffin. Sections 3-5 μm in thickness were stained with hematoxylin and eosin, according to van Gieson, and iron hematoxylin according to Heidenhain. Calcium salts were demonstrated according to Koss.

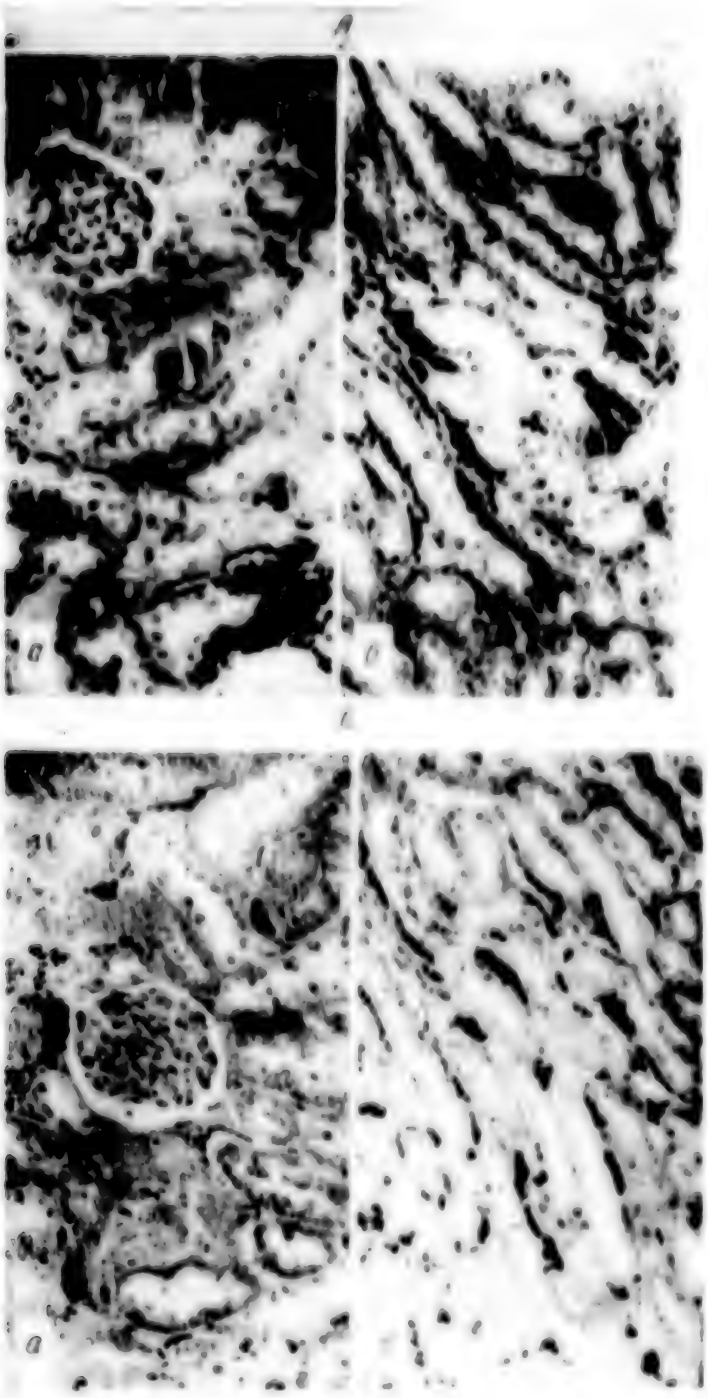
Table 1. Relative weight (mg/100 g body weight) of rat kidneys after flight aboard Cosmos-936 biosatellite (M¹m, 4.5-13 h after landing)

Parameter	Group of animals				
	1	2	3	4	5
Number of rats	10	4	10	5	10
Kidney weight	934 ± 24.4	859 ± 21	731 ± 15.3	843 ± 21	736 ± 12.6
P	$P_1 < 0.05$ $P_2 < 0.001$ $P_3 < 0.001$	$P_2 < 0.001$ $P_3 < 0.001$	$P_3 < 0.002$	$P_4 < 0.02$	

Note: Here and in Table 2, the value of P reflects differences between groups bearing the indicated numbers.

Results and Discussion

There was an increase in weight of the kidneys of animals in the first group sacrificed right after landing, as compared to animals in the 3d, 4th and 5th groups (Table 1). There was less marked increase in kidney weight of rats in the 2d group than in the 1st. Thus, it can be concluded that creation of artificial gravity during the flight attenuated the effect of weightlessness. In the experiments where gravity constituted 1.4 G under ground-based conditions (4th group), there was also an increase in weight of the kidneys, and it was close to that of rats in the 2d group.



Plethora of juxtamedullary glomerules (a) and rectus vessels (б) of renal medullary substance in rats of the 1st (А) and 2d (Б) groups

Table 2. Relative weight (mg/100 g body weight) of rat kidneys after flights aboard Cosmos series of biosatellites (M±m)

Parameter	Cosmos-605			Cosmos-782			Cosmos-936		
	1	2	3	1	2	3	1	2	3
Number of rats	11	15	20	12	12	11	10	10	10
Kidney wt	837±18	683±12	695±8	900±20	680±10	700±10	938±21.1	733±15.0	736±12.6
P	$P_2<0.001$ $P_3<0.001$			$P_2<0.001$ $P_3<0.001$			$P_2<0.001$ $P_3<0.001$		

Key: 1) weightlessness 2) ground-based experiment 3) vivarium control

No differences in kidney weight were observed in animals sacrificed 25 days after the flight (there was the same number of animals as in the groups sacrificed at the early stages).

We first observed an increase in weight of the kidneys among Wistar rats flown aboard Cosmos-605 for 20.5 days [8].

Since such an increase in kidney weight occurred consistently in subsequent flights aboard satellites of the Cosmos series, we submitted the data to a comprehensive analysis. In rats sacrificed on the 1st postflight day, after flight aboard Cosmos-605 biosatellite, the increase in weight of the kidneys constituted 20.6% of the vivarium control and synchronous experiments; in animals sacrificed on the 2d postflight day, this parameter increased by 26%. In rats sacrificed 5-13 h after flights aboard Cosmos-782 and Cosmos-936, the increase in kidney weight constituted 28 and 26%, respectively (Table 2). We were unable to demonstrate the dynamics of increase in kidney weight with increase in time after returning to earth within that interval. Thus, the increase in renal weight remained stable in the interval of several hours to 2 days after returning to earth (20-28%).

The significant increase in weight of kidneys in the first hours after the flight suggests that it occurred during weightlessness. However, we could not demonstrate the corresponding morphological changes with the methods we used. There were no marked dystrophic changes in tubular epithelium or signs of hypertrophy of glomerular elements. For this reason, it is more probable that the increase in weight occurred acutely during adaptation of animals from weightlessness to earth's gravity. Such

a rapid increase in kidney weight cannot be attributed to an increase in weight of the parenchyma, since it is known from data in the literature that, in the case of such a potent factor as removal of a kidney, a 20% increase in dry weight of the other kidney occurs only 72 h after nephrectomy, and a 30% increase occurs 120 h after this operation [10]. It remains for us to assume that this is related to changes in hemodynamics and fluid content of this organ. Indeed a special study of functional capillaries revealed morphological signs of hemodynamic disturbances. Anemia of cortical vessels was demonstrated in the 2d group of rats: cortical capillaries were collapsed over a significant distance, and contained virtually no erythrocytes. There was nonuniform filling of glomerular capillaries: they were anemic in the superficial zone of the cortex, whereas juxtamedullary glomerules were appreciably enlarged due to plethora of capillary loops (Figure 1Aa). We were impressed by the severe plethora of rectus vessels of the medulla, which were arranged in parallel chains and contained many erythrocytes in their lumen (Figure 1Ab). It must be noted that the plethora of juxtamedullary glomerules and medullary vessels increased with increase in time after returning to earth, and it was the most marked in rats sacrificed 8-10 h after the flight.

Thus, there was development of renal blood flow over a shortened juxtamedullary route in rats that returned to earth's gravity after weightlessness. This change is nonspecific, and it occurs in many stress situations. We observed it in animals exposed to longitudinal and transverse accelerations of 4 G [11]. In this experiment, the change from weightlessness to conditions on earth can also be interpreted as exposure to accelerations. This is indicated by observations that animals flown aboard biosatellites with AG presented nonuniform filling of vessels in different parts of the cortex and plethora of rectus vessels of the medullary substance, both findings being insignificantly expressed. Juxtamedullary glomerules were not as large as in animals submitted to weightlessness (Figure 1Ba, and b). The intensification of morphological signs of blood flow shunting in the kidneys of the 1st group of rats with increase in time of return to earth's conditions also confirms the fact that redistribution of blood is due to the change from weightlessness to earth's gravity. Activation of the renin-angiotensin system is one of the mechanisms that intensifies blood flow via the juxtamedullary route. Although the juxtaglomerular apparatus of the kidneys was not examined in this experiment, we have information indicative of increased activity thereof in rats sacrificed on the 2d day after the flight aboard Cosmos-605 [8]. We also observed an increase in activity of the renin-angiotensin system in experiments on rats submitted to accelerations of 4 G [12]. It is known that the reduction of renal blood flow under extreme conditions is instrumental in retention of fluid and electrolytes, and it implies that there is a decrease in diuresis.

According to current conceptions the retention of fluid and salts observed in cosmonauts on the first few days after returning to earth was due to hypohydration, which developed in weightlessness as a result of

redistribution of blood [1]. It is difficult to state whether there is loss of fluid in weightlessness by rats, animals whose natural body position is horizontal. It would be wrong to answer this question categorically in the negative, since we consider it an incomplete explanation to attribute retention of fluid and electrolytes with the change from weightlessness to earth's gravity to intensification of cutaneous and pulmonary elimination ["expenditures"] [7]. One could hardly attribute the maximum decrease in sodium and potassium excretion, which Ilyushko et al. observed [6] on the 4th and 5th postflight days, solely to increase in extrarenal loss. Evidently, there is impairment of ion-regulating function of the kidneys and a change in hormonal balance in rats returning to earth after flights aboard biosatellites.

Thus, the comparative analysis revealed that there was a statistically reliable and equally marked increase in kidney weight of rats flown aboard Cosmos-605, Cosmos-782 and Cosmos-936 biosatellites on the first 2 postflight days. The presence of artificial gravity aboard Cosmos-936 led to a less marked increase in kidney weight. We are still far from having a definitive answer as to the mechanisms that lead to the increase in kidney weight, but we believe that one of the possible causes is the increase in filling with blood and concomitant development of juxtamedullary blood flow. It is known that the rate of glomerular filtration is higher in juxtamedullary nephrons than in superficial ones [13]. At the same time, there is a distinct positive correlation between rate of filtration and kidney weight, not only in rats [14], but in other mammals [15].

Consequently, in our case the increase in weight of the kidneys could be related to an increase in blood flow, which means also an increase in rate of filtration in the nephrons. We cannot rule out the possibility that, when blood flow is shunted, there is shifting of fluid from the vascular bed into the interstitial space, which could also lead to an increase in weight of the kidneys.

BIBLIOGRAPHY

1. Natochin, Yu. V., et al. KOSMICHESKIYE ISSLEDOVANIYA [Space Research], Vol 3, No 6, 1965, pp 935-939.

2. Grigor'yev, A. I. in "Funktsional'noye sostoyaniye pochki pri ekstremal'nykh usloviyakh" [Functional State of the Kidney Under Extreme Conditions], Leningrad, 1976, pp 131-149.

3. Grigor'yev, A. I., and Kozyrevskaya, G. I. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1970, pp 55-59.

4. Balakhovskiy, I. S. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 22, 1973, pp 89-167.

5. Berry, Ch. A. in "Man in Space," Moscow, 1974, pp 51-70.

6. Ilyushko, N. A.; Il'in, Ye. A.; Korol'kov, V. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 1, 1975, pp 12-14.

7. Ilyushko, N. A., and Kondrat'yev, Yu. I. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, p 28.

8. Savina, Ye. A.; Pankova, A. S.; and Alekseyev, Ye. I. KOSMICHESKAYA BIOL., No 5, 1977, pp 72-76.

9. Il'in, Ye. A.; Korol'kov, V. I.; and Kotovskaya, A. R. Ibid, No 6, 1979, pp 18-22.

10. Johnson, H. A., and Vera Roman, J. M. AM. J. PATH., Vol 49, 1966, pp 1-13.

11. Savina, Ye. A., and Pankova, A. S. KOSMICHESKAYA BIOL., No 3, 1973, pp 8-12.

12. Pankova, A. S. Ibid, No 6, 1972, pp 19-23.

13. Tucker, B., et al. AM. J. PHYSIOL., Vol 232, 1977, pp 97-104.

14. DeRouffignac, C., et al. J. PHYSIOL. (London), Vol 262, 1976, pp 119-129.

15. Bankir, L., et al. PFLUG. ARCH., Vol 366, 1976, pp 89-93.

UDC: 616.24-091-02:629.78

MORPHOLOGICAL CHANGES IN RAT LUNGS AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1980 pp 31-35

[Article by V. I. Yakovleva, submitted 4 Jan 79]

[English abstract from source]

Lungs of 20 rats flown aboard Cosmos-936 for 18.5 days and sacrificed within 5-13 hours (8 weightless and 4 centrifuged rats) and 25 days (4 weightless and 4 centrifuged rats) after recovery were studied histologically. An identical number of lung specimens were withdrawn from rats of synchronous and vivarium controls. Lungs of the flight rats did not show any pathological changes or morphological signs of prolonged congestion, thus indicating the lack of hypertension in pulmonary circulation. Lungs of the flight rats exhibited an increased leukocyte count, which was more marked in the weightless rats killed 8-13 hours postflight. The elevation in the count of neutrophilic leukocytes in the flight rats was due to peripheral neutrophilia which is a manifestation of an acute stress-reaction. An exposure of rats to artificial gravity was responsible for a lesser increase in the count of neutrophilic leukocytes.

[Text] No pathological changes in the pulmonary parenchyma related to the effects of space flight factors were demonstrated in a histological examination of rat lungs following flights aboard Cosmos-605 and Cosmos-690 [1-3]. An increase in number of neutrophil leukocytes in pulmonary vessels and interalveolar septa was found in animals flown aboard Cosmos-782. There was a particularly marked increase in neutrophil leukocytes at the later postflight stages (after 8-11 h). These findings made it possible to relate the increase in number of leukocytes to neutrophilia of peripheral blood, reflecting an acute stress reaction. The results of biochemical and morphological studies are indicative of presence of signs of an acute stress reaction in rats in the first postflight hours [4-7].

In the experiment aboard the Cosmos-936 biosatellite, it was interesting to conduct comparative studies of morphological manifestations of the stress reaction in the lungs of rats that had been in weightlessness and exposed to artificial gravity (AG) of 1 G.

Methods

We took samples of lung tissue from 20 SPF Wistar rats, which had spent 18.5 days aboard Cosmos-936, for histological examination. We sacrificed 8 rats which had been in weightlessness and 4 which had been exposed to AG within the first 5-13 h after the flight, and 4 animals from each group 25 days after the flight. As a control, we used the same number of specimens of lung tissue from rats used in the corresponding ground-based model experiments and the vivarium control. The experimental conditions have been described in detail elsewhere [8]. In all of the above groups, we examined rat lungs presenting no inflammatory changes.*

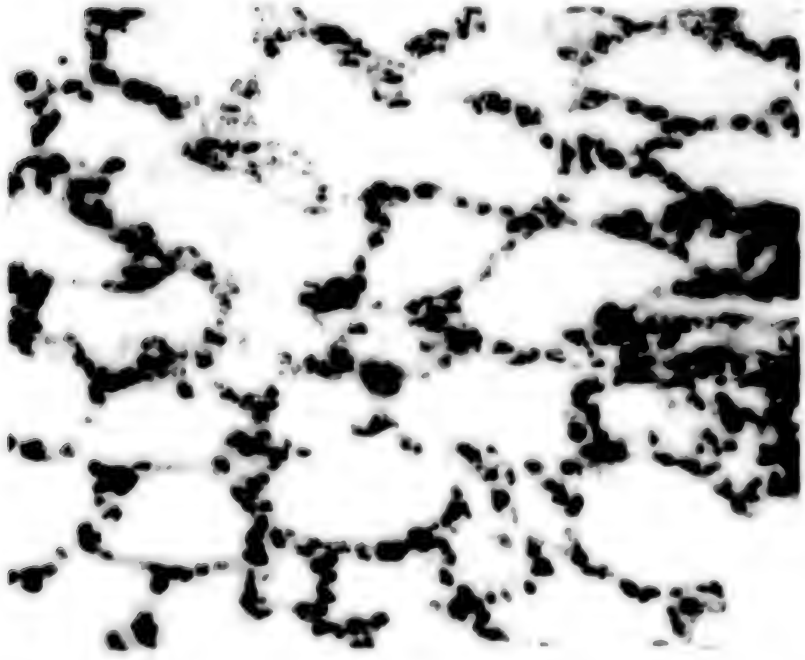


Figure 1. Lung of intact control animal. Here and in Figures 2 and 3: 10% neutral formalin; hematoxylin-eosin; objective 40× ocular 10×

Lung samples were fixed in 10% neutral formalin and embedded in paraffin. The preparations were stained with hematoxylin and eosin, according to van Gieson, Weigert, and we ran the reaction for iron according to Perls.

*Chronic interstitial pneumonia was demonstrated in 17 out of the 74 rats examined.

The Goldman method was used for demonstration of neutrophil leukocytes. The number of leukocytes was determined visually and graded on a 4-point system, from + (few) to ++++. Mast cells were stained with toluidine blue. We counted cells per longitudinal sections of the left lung and passing through the hilus. The digital data were processed by the method of variation statistics. The results were considered reliable with $P<0.05$. Reliability of differences was determined by the criterion of Student.

Results and Discussion

No differences were demonstrated in filling of vessels in samples of rat lungs taken 5-13 h after the flight, as compared to rats in ground-based model experiments and intact animals. There was more distinct capillary plethora in the lungs of only two rats exposed to AG and all animals rotated on the centrifuge in the ground-based experiment.

A special study revealed that there was a difference in neutrophil leukocyte content of lung tissue of animals in different groups. The highest number of leukocytes (++++) was demonstrated in the lungs of rats that had been submitted to weightlessness and were sacrificed 9-13 h after the flight. In these animals, accumulations of segmented nuclears were found in the lumen of large vessels, perivascular tissue, as well as capillaries of interalveolar septa, with exit of the latter into the alveolar lumen. In lung samples taken at an earlier postflight time (5-8 h), there were fewer (+++) neutrophils, and they were localized mainly in the septal capillaries. The process of migration beyond the capillaries had only begun (Figures 1-3). The leukocyte count was lower (+++ or ++) in rats rotated on the centrifuge and sacrificed 5-8 h after the flight than in animals in the weightlessness group at the same times. We failed to demonstrate clearcut dynamics of increase in leukocyte count in rats used in the ground-based experiment with increase in interval after which they were sacrificed, while the total leukocyte count was lower (++) than in the flight groups of rats.

The leukocyte count of lung tissue of rats in all experimental groups did not differ 25 days after the flight and after termination of ground-based experiments from the count of animals in the vivarium control.

There was a decrease in number of mast cells in rats flown aboard Cosmos-605 and Cosmos-690 2 days after the flight [1-3]. For this reason it was interesting to count the mast cells at earlier postlanding stages.

It is known that there is a significant change in number of mast cells during development of adaptative reactions and in the presence of various pathological states [9-14]. There are indications by a number of authors that mast cells react to stress factors [15-17]. According to the data of these researchers, an acute stress state leads to a decrease in number of connective tissue mast cells, whereas prolonged (chronic) stress is associated with an increase in number of mast cells. A particularly drastic

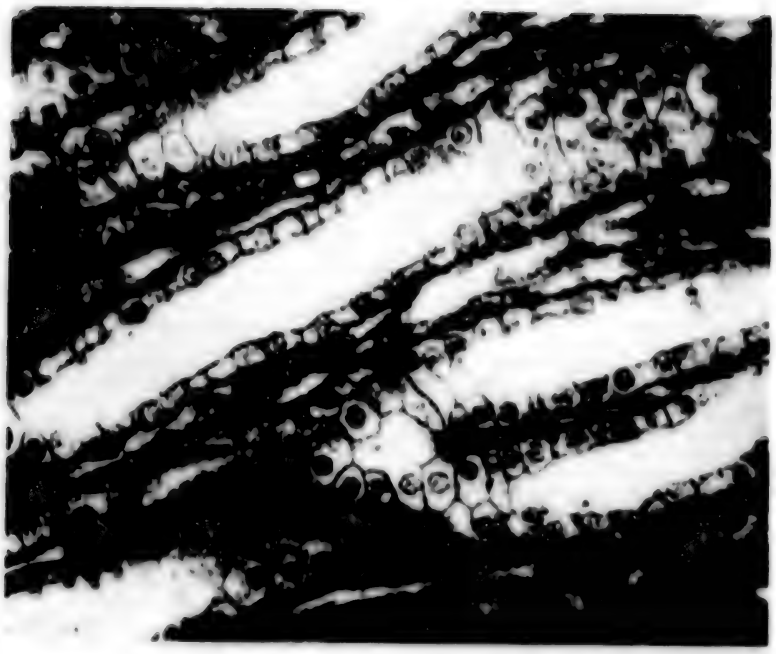


Figure 2. Moderate number of neutrophils in interalveolar septa of the lung 5 h after the flight

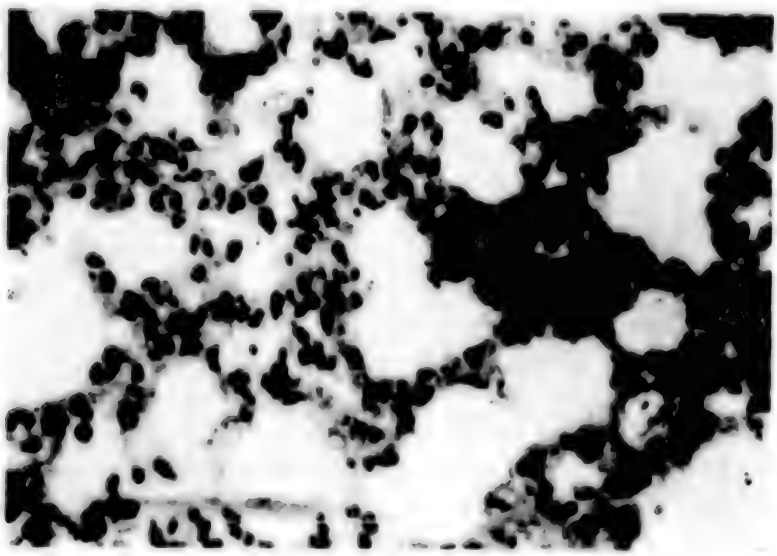


Figure 3. Marked increase in number of neutrophils in lung tissue 12 h after the flight

increase in number of mast cells is observed in the lungs in the presence of stasis in the pulmonary circulation [13, 14]. For this reason, the study of mast cells of the lungs was of interest, both from the standpoint of the reaction of lung tissue to stressors and to assess the hemodynamics of the lungs. We failed to demonstrate reliable differences in number of mast cells in the lungs of animals that had been submitted to weightlessness, as compared to the vivarium control (236±45 for the weightlessness group and 198±32 for the vivarium control; $P<0.01$).

Analysis of the results of counting mast cells of rats submitted to rotation on a centrifuge in flight and ground-based experiments revealed wide individual variations in their number. It is known that the number of mast cells fluctuates over a wide range in rats of the same sex and age [18]. It should be noted that, of all the experimental and control groups of animals sacrificed at the two different times, widest variability in number of mast cells was observed expressly in rats submitted to rotation on centrifuges. Thus, the total number of mast cells ranged from 351 to 585 in rats submitted to artificial gravity, 196 to 461 in those exposed to gravity of 1.4 G in the ground-based experiment and 162 to 421 in those rotated on a short-arm centrifuge.

The mast cell content of lung tissue in all experimental groups did not differ from control values 25 days after the flight and completion of ground-based experiments.

Thus, the results of this study revealed that there were no pathological changes or morphological signs of persistent circulatory disturbances in the lungs of rats sacrificed 5-13 h and 25 days after termination of the flight. This warrants the belief that the insignificant increase in number of mast cells in both flight groups of animals 5-13 h after the flight was unrelated to chronic pulmonary stasis, in the presence of which, as we know, the number of mast cells increases by many times [14]. It is difficult to determine the cause of the insignificant increase in number of mast cells in the above-mentioned groups. It must be noted that a decrease in number of mast cells was demonstrated only 2 days after landing in the lungs of rats flown aboard Cosmos-605 and Cosmos-690. At that time, the decrease in number of mast cells was interpreted as a manifestation of a readaptation reaction [1-3]. One would think that there had not been time for the mast cell reaction to develop in the lungs of rats flown aboard Cosmos-936 by the time the animals were sacrificed (examination performed 5-13 h after completion of the flight). The drastic fluctuations in number of mast cells in the lungs of rats rotated on centrifuges are apparently a reflection of the animals' individual reactions to rotation factors.

The increase in number of neutrophils in pulmonary vessels and tissues of rats in the flight experiment that were sacrificed at the earlier time was attributable to neutrophilia of peripheral blood, which is one of the manifestations of an acute stress reaction. It must be noted that the most marked increase in leukocyte count was found in animals from the weightlessness group, which were sacrificed at the later postflight time

(9-13 h). The results of morphological examination of the adrenals and lymphoid organs [6, 7], as well as of biochemical studies of corticosterone content of blood plasma and adrenal tissue [4, 5], are indicative of development of an acute stress reaction in rats in the first postflight hours.

According to the number of neutrophils in the lungs, the manifestation of the stress reaction was less marked in animals kept under conditions of artificial gravity than in those submitted to weightlessness.

BIBLIOGRAPHY

1. Katunyan, P. I. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, Vyp 2, 1975, pp 96-98.

2. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1974, pp 19-25.

3. Portugalov, V. V., and Savina, Ye. A. Ibid, No 1, 1978, pp 17-22.

4. Tigranyan, R. A.; Popova, I. A.; Belyakova, M. I.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 9-y. Materialy" [Proceedings of 9th Symposium on Space Biology and Medicine], Budapest, 1976, p 83.

5. Kvetnyanski, R.; Tigranyan, R. A.; Torda, T.; et al. Ibid, pp 100-101.

6. Savina, Ye. A. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, pp 58-59.

7. Durnova, G. N.; Kaplanskiy, A. S.; and Portugalov, V. V. ARKH. ANAT. [Archives of Anatomy], No 5, 1977, pp 14-20.

8. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL., No 6, 1979, pp 18-22.

9. Danilova, K. M. ARKH. PAT., No 1, 1958, pp 3-12.

10. Morozova, M. M. in "Aktual'nyye voprosy patologii" [Pressing Problems of Pathology], Moscow, 1968, pp 295-304.

11. Linder, D. P., and Kogan, E. M. ARKH. PAT., No 8, 1976, pp 3-14.

12. Niebauer, G. ARCH. KLIN. EXP. DERM., Vol 213, 1961, pp 556-565.

13. Kay, J. M.; Gill[illegible]; and Heath, D. AM. J. PATH., Vol 51, 1967, pp 1031-1044.

14. Heath, D.; Trueman, T.; and Sukonthamarn, P. CARDIOVASC. RES., Vol 3, 1969, pp 467-471.

15. Selye, H. "The Mast Cells," Washington, 1965.

16. Kolodeznikova, Ye. D. in "Mediko-biologicheskiye aspekty protsessov adaptatsii" [Biomedical Aspects of Adaptation Processes], Novosibirsk, 1975, pp 160-162.

17. Meleshin, S. V., and Meleshina, O. B. Ibid, pp 285-287.

18. Vinogradov, V. V., and Vorob'yeva, N. F. "Mast Cells (Genesis, Structure and Functions)," Novosibirsk, 1973, pp 5-104.

UDC: 629.78:612.398.145.1.014.24:576.315.42

TEMPLATE ACTIVITY OF CHROMATIN DNA AND THE ADENYLATE CYCLASE SYSTEM OF RAT TISSUES FOLLOWING FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1980 pp 35-38

[Article by Ye. N. Troitskaya, V. P. Makeyeva, G. S. Komolova, I. A. Yegorov and R. A. Tigranyan, submitted 22 Feb 79]

[English abstract from source]

Chromatin DNA template activity and cAMP metabolism enzymes in the liver and lymph organs of rats flown for 19 days were studied. Postflight RNA synthesis on the chromatin DNA template was increased in the liver and decreased in lymph organs. Adenylate cyclase and phosphodiesterase activities decreased in the liver and increased in lymph organs. No correlation between cAMP enzyme activity and chromatin DNA template activity was found. The nature of the biochemical changes in animal tissues is discussed.

[Text] It was previously [1] established that reversible changes occur in the nucleic acid system of animal tissues following space flights; these changes are apparently related to formation of compensatory and adaptive reactions to the extreme environmental conditions.

This study deals with demonstration of the mechanism of effects of space flight factors on RNA of animal liver and lymphoid organs. In view of the fact that the intensity of RNA synthesis depends primarily on template activity of DNA in the RNA polymerase system, we also studied this parameter. Cyclic nucleotides play an important part in regulation of metabolism, as well as functional activity of nucleic acids [2-4]. We studied the activity of enzymes of cAMP metabolism--adenylate cyclase and phosphodiesterase.

Methods

Experiments were conducted on 3 groups of male Wistar rats (5 animals in each group). The 1st group consist of rats kept in the vivarium (control); the 2d consisted of animals used in a synchronous experiment, and the 3d consisted of rats that were flown aboard Cosmos-936 for 19 days. Control

animals were kept on the same diet as experimental ones; the 2d group of rats had the same life support systems (LSS) as the flight animals (3d group).

The animals were decapitated 10 h after the flight or removal from LSS. After freezing in liquid nitrogen and transportation in dry ice, the extracted organs (liver, spleen, thymus) were analyzed. A modification of the method of Marushige and Bonner [5] was used to isolate chromatin from the liver, spleen and thymus. Template activity of chromatin preparations was determined in an acellular system of E. coli RNA polymerase by the method of Cedar and Felsenfeld [6]. Chromatin (2 μg) in the presence of RNA polymerase (5 units) was kept for 15 min at 37°C in 0.5 mℓ incubation mixture of the following composition: 20 mmole tris-HCL, pH 7.9; 1 mmole $MnCl_2$; 0.2 mmole each of ATP and GTP, and 0.02 mmole ^{3}H-UTP (specific radioactivity 1 Ci/μmole). The initiation reaction was stopped with 0.4 M $(NH_4)_2SO_4$. Growth of the RNA chain began upon addition of 5 mmole MgCl and 0.2 mmole CTP [cytidine triphosphate]. Intensity of RNA synthesis was assessed according to incorporation of labeled UTP in its molecules. To analyze radioactivity, the samples were applied to glass filters (Whatman GF/A) and successively washed off with 15 mℓ 5% trichloroacetic acid with 0.5% sodium pyrophosphate and 3 mℓ 70% ethanol.

To determine enzyme activity, a 10% homogenate was prepared from tissues at 4°C in 50 mM tris-HCl buffer, pH 7.6, containing 0.25 M saccharose and 10 mM $MgSO_4$. The homogenate was centrifuged at 2000 G for 20 min. Phosphodiesterase (PDE) was assayed in the supernatant. The precipitate was resuspended in tris-HCl buffer and used to demonstrate adenylate cyclase (AC). PDE activity was determined radiometrically, according to rate of hydrolysis of cAMP to 5'-AMP. The reaction mixture (total volume 50 μℓ) was of the following composition: tris-HCl buffer, pH 7.7 and 8.4, for the liver and spleen, respectively; 3 mM $MgSO_4$, 2 mM cAMP, 1.0 μCi/μℓ ^{3}H-cAMP (Amersham), 6-8 mg/mℓ protein. Incubation was performed in microtubes for 30 min at 30°C. The reaction was stopped by boiling for 3 min. The coagulated protein was removed by centrifugation (10 min, 2500 G). The supernatant was used to separate nucleotides on silufol planchets [7]. The fluorescent spots were cut out, put in 0.5 mℓ water overnight and, after addition of 10 mℓ Bray mixture [8], radioactivity was measured. Activity of PDE was determined according to decrease in reaction substrate per unit time, and it was expressed in nmole/mg protein per min.

The method of measuring AC activity is based on the enzymatic reaction of formation of cAMP from ATP. The reaction mixture (tris-HCl buffer, pH 7.6; 2 mM ATP, 3 mM $MgCl_2$, 10 mM caffeine, 10 mM NaF, 0.015% bovine serum albumin, 20 mM phosphocreatine, 2 mg/mℓ creatine kinase, 6-8 mg/mℓ protein) in a volume of 100 μℓ was incubated for 15 min at 30°C. cAMP was determined according to binding with protein, using standard sets of the Amersham Company. We assayed protein in the samples by the method of Lowry [9]. Activity of the enzyme was determined from the increment of cAMP in picomoles/mg protein/min. In all cases, radioactivity of the samples was measured using an SL-30 liquid scintillation counter (France).

Results and Discussion

The data listed in Table 1 indicate that uptake of ^{3}H-UTP in the hepatic RNA of animals in the flight and synchronous experiments was higher than in the vivarium control. Apparently, the increase in chromatin DNA template activity in the RNA polymerase system is attributable to stress factors, since we know that there is an increase in intensity of synthesis of cytoplasmic and nuclear RNA under the influence of glucocorticoids released from the adrenal cortex in stress situations [10, 11]. Unlike the liver, the space flight and synchronous experiment factors lower the rate of incorporation of the tracer in chromatin RNA of lymphoid organs, and this decline is more marked for the spleen in the flight experiment and for the thymus in the synchronous one. It is known that hypoplasia of lymphoid organs is observed under stress conditions [12]. The obtained data on decrease in DNA template activity are consistent with this fact. According to the parameter of intensity of RNA synthesis on a nuclear chromatin DNA template, it can be concluded that there are no appreciable differences between the effects elicited by flight factors and synchronous experiment conditions.

Table 1. Template activity of rat tissue chromatin DNA

Animal group	^{3}H-UTP uptake in cell RNA (M±m), percent of control		
	liver	thymus	spleen
First	100±10	100±3	100±4
Second	187±12 ($P_1<0.05$)	66±3 ($P_1<0.05$)	90±3 ($P_1>0.05$)
Third	144±11 ($P_1=0.05$) ($P_2>0.05$)	90±5 ($P_1>0.05$) ($P_1=0.05$)	68±5 ($P_1<0.05$) ($P_2>0.05$)

Note: Here and in Tables 2 and 3, $P_{1,2}$ is the reliability index for the first and second groups, respectively

Table 2. AC activity in rat tissues

Animal group	cAMP, nmole/mg protein/min	
	liver	spleen
First	121.7±5.4	169.6±3.8
Second	95.2±7.9 ($P_1=0.05$)	184.1±6.7
Third	99.1±7.7 ($P_1>0.05$)	203.3±8.2 ($P_1>0.05$)

Table 3. PDE activity in rat tissues

Animal group	cAMP, nmole/mg protein/min	
	liver	spleen
First	5.1±0.2	0.40±0.1
Second	5.1±0.3	0.70±0.30
Third	4.6±0.3	0.20±0.12
	($P_{1,3}>0.05$)	($P_{1,3}>0.05$)

Table 2 shows that liver AC activity decreases both after the flight (by about 19%) and after the synchronous experiment (by approximately 23%). Conversely, there is some tendency toward activation of this enzyme in the spleen of animals in the third group (however, the differences from the vivarium control are statistically unreliable). PDE activity is diminished with statistical unreliability (by about 15%) in the liver of the third group of animals (Table 3). After the flight, there is some tendency toward increase in activity of this enzyme in the spleen. In the synchronous experiment there is virtually no effect. Thus, with regard to AC and PDE activity, the tissues examined were not very sensitive to space flight factors. The tendency toward some decline in the liver and increase in the spleen applies to virtually the same extent to enzymes involved in anabolic (AC) and catabolic (PDE) aspects of cAMP metabolism. For this reason, it should be assumed that only the intensity of cAMP metabolism (synthesis and degradation simultaneously) may change under the influence of space flight factors, while the level thereof in tissues should remain unchanged. In view of the lack of significant differences between the results of the synchronous and flight experiments, it can be assumed that the weightlessness of space does not have any specific influence. At the same time, data obtained from the experiments indicate that, with regard to template activity of chromatin DNA, the liver and lymphoid organs behave in a manner that is typical of stress situations after the flight and synchronous experiment. The absence of correlation between the changes in intensity of RNA synthesis on the DNA template and activity of enzymes of cAMP metabolism induced by flight factors and LSS merits attention. Since corticosteroid hormones express their action without the involvement of cyclic nucleotides, there is confirmation of the conclusion that the changes in the nucleic acid system of the liver and lymphoid organs of animals demonstrated after the space flight are referable to stress.

BIBLIOGRAPHY

1. Komolova, G. S.; Guseynov, F. T.; Makeyeva, V. F.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1977, pp 17-19.

2. Short, J.; Tsukada, K.; Rudert, W. A.; et al. J. BIOL. CHEM., Vol 250, 1975, pp 3602-3606.

3. Ebina, Y.; Iwai, H.; Fukui, N.; et al. J. BIOCHEM. (Tokyo), Vol 77, 1975, pp 641-645.

4. Rechler, M. M.; Bruni, C. B.; Podskalny, J. M.; et al. J. SUPRAMOL. STRUCT., Vol 4, 1976, pp 199-204.

5. Marushige, K., and Bonner, J. J. MOLEC. BIOL., Vol 15, 1966, pp 160-174.

6. Cedar, H., and Felsenfeld, G. Ibid, Vol 77, 1973, pp 237-254.

7. Beritashvili, D. R., and Kafiani, K. A. VOPR. MED. KHIMII [Problems of Medical Chemistry], Vol 21, -975, pp 322-324.

8. Bray, G. A. ANALYT. BIOCHEM., Vol 1, 1960, pp 279-285.

9. Lowry, O. H.; Rosebrough, N. J.; Farr, A. L.; et al. J. BIOL. CHEM., Vol 193, 1951, pp 265-267.

10. Argutinskaya, S. V.; Knorre, V. L.; Yefimova, L. Yu.; et al. MOLEKULYARNAYA BIOL. [Molecular Biology], No 6, 1973, pp 802-809.

11. Yudayev, N. A. in "Novoye o gormonakh i mekhanizme ikh deystviya" [News About Hormones and Mechanism of Their Action], Kiev, 1977, pp 51-65.

12. Gorizontov, P. D., and Zimin, Yu. I. in "Aktual'nyye problemy stressa" [Pressing Problems of Stress], Kishinev, 1976, pp 70-79.

UDC: 613.693-07:612.821.2+612.275.1.017.2:612.821.2

EFFECTS OF TRANSMERIDIONAL FLIGHTS AND HIGHLAND CONDITIONS ON DIFFERENT FORMS OF MEMORY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 38-41

[Article by R. Yu. Il'yuchenok, L. A. Konstantinovskaya and N. I. Dubrovina, submitted 26 Oct 78]

[English abstract from source]

The effect of transmeridional flights and highland exposure on memory processes was studied. During 21-day observation following an environmental change memory processes were activated, short-term memory storage increased, proactive and retroactive interference decreased, fixation of memory track improved, number of remembered errors and forgetfulness lessened. These processes were especially active during 11th through 21st days of adaptation. Improvement of short-term memory was found in visual and acoustic tests, perturbed short-term memory being changed more significantly. These findings point to the leading role of memory in the development of adaptive behavioral programs. The conclusions can be applied to the selection of optimal mental tasks given to the man after his transmeridional flight or transfer to highland.

[Text] The study of the role of memory in the adaptation process is drawing increasing attention on the part of researchers [1-5]. The capacity to alter one's behavior in accordance with acquired experience is considered to be a most important factor of individual adaptation of higher animals and man to altered conditions [4].

In this article, we submit the results of a study of changes in memory processes of man over a period of 21 days following a transmeridional flight with a 4-h time zone shift and in the course of a 21-day stay in the highlands (altitude 2500 m).

Methods

A total of 15 men and women (chiefly scientists) ranging in age from 19 to 47 years participated in this study. No age differentiation was made in processing the data.

The program included 5 tests (on the 2d, 3d, 4th, 11th and 21st days) under the same conditions and using the same procedures.

We tested verbal short-term memory (SM) with the use of words (15 per list) and syllables (10 per list) according to the change in immediate recall at a reading rate of 1 word (syllable) per second. The lists were prepared with due consideration of the frequency of words used in the Russian language, as well as with maximum exclusion of direct associations between words and of consonance of syllables.

Long-term memory (LM) was tested by means of memorizing a list of 20 adjectives to 75% retention, with subsequent recall 24, 48 and 72 h later and recognition (after 72 h). The memorizing process was analyzed according to the change in number of trials required to remember 75% of the words.

Figurative and spatial SM (FS SM) was studied according to the change in number of correctly remembered locations of a black square on five successively presented cards (total of 3 series). The number of squares on the card constituted 5×5; exposure time was 1 s, interval between presentations of cards was 1 s and the interval between series was 2 min. Corner and middle squares were not used.

To study proprioceptive motor SM (PM SM), the method developed in our laboratory was used, and the subjects had to reproduce a height specified in the range of 95-135 cm (95, 100, 105, etc.).

The sequence of heights was determined from the table of random numbers. Placing the hand, with the edge of the palm on a specific mark on a four-sided [tetrahedral] rod, the researcher issued the command "height" and the subject, looking straight ahead, raised his hand to the stop (the investigator's hand) on the rod situated on the left for the left hand and on the right for the right hand. In this variant, visual correction of height is ruled out. The time of fixation of height was 1 s; then, in response to the commands to "drop the hand" and "raise the hand," the subject reproduced the specified height.

Proactive (PA) and retroactive (RA) interferences and reminiscences were tested by methods described previously [6]. The level of immediate recall obtained on the same day by the method of determining SM served as a control in determining the PA and RA levels.

The results of control tests (at least 3 by each method) revealed that there was no tendency toward increment of parameters with increase in number of tests.

The obtained data were submitted to statistical processing using the criteria of Student and Fisher for dependent samples and the sign criterion [7, 8]. The validity of using parametric criteria for a given sample was tested by the nature of distribution of various parameters that were close to normal.

Results and Discussion

Table 1 illustrates the dynamics of parameters of different forms of SM. As can be seen in Table 1, during the test period, there is an increase in volume of verbal SM, but the dynamics of changes in SM of words and syllables differed somewhat. M. M. Mirrakhimov et al. observed stable improvement of memory after the 10th day of adaptation to high altitude [9]. However, for the first few days, the changes in verbal SM were unstable, and it improved in only half the subjects. The insignificant dominance of contribution of "improved" parameters was sufficient for the mean group SM (word) index to become reliably above the control value on the 3d day, with negligible dispersion of control values. According to M. M. Mirrakhimov et al. [9], improvement of memory on the 2d day of adaptation to the highlands was manifested by a reliable increase in number of reminiscences and unreliable increase in volume of immediate ["operational"] memory. Thus, while improvement of memory after the 10th-11th day is convincing, the initial changes in memory are not indisputable. It is not deemed possible to derive a definitive conclusion as to the nature of such SM changes at this time.

Table 1. Dynamics of SM (number of correct reproductions) at a high altitude (2500 m)

Parameter	Control	Days				
		1	3	4	11	14
SM (words)						
PM (syllables)						
FS SM						

Note: Here and in Tables 2 and 3: asterisks indicate that $P<0.05$.

The dynamics of FS SM are shown in Table ': from the 3d day to the end of the test it was above control levels.

Interestingly enough, during the adaptation period there was a 26% increase in nonverbal SM (4th day), whereas verbal SM increased by only 12% (11th day). If we consider the significance of dominance of the left hemisphere in processing of verbal information and that of the right hemisphere for nonverbal information [10], this finding may be indicative of greater activation of the right hemisphere than the left, i.e., increased functional asymmetry of the hemispheres during the adaptation period.

In this regard, the changes in PM SM are interesting. The dynamics of PM SM while performing tasks with the right and left hand during the adaptation period differed in direction: from the 2d day of adaptation on, there was a change in parameters for the left hand ($P<0.05$) in the direction of increase in deviation of height from the specified level, and they revert

to normal by the end of the period; the parameters for the right hand change in the direction of decrease in absolute difference between specified and reproduced height, and by the end of the period they deviate by 10% from the control value.

Table 2. Dynamics of changes in LP (number of correct reproductions) after transmeridional flight and with acclimatization to high altitude (2500 m)

LM parameter	Transmeridional flight			Mountains		
	control	memorizing, day		control	memorizing, day	
		3d	11th		3d	21st
Deferred reproduction: 24 h	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
48 h	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
72 h	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Recognition (after 72 h)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	—

Table 3. Dynamics of memorizing list of words after transmeridional flight and with acclimatization to high altitude (2500 m)

Parameter	Transmeridional flight			Mountains		
	control	day		control	day	
		3d	11th		3d	21st
First reproduction	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of tests	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

At the initial stage (2d-3d day), there is an increase in individual scatter ($P<0.05$), with normalization toward the end of the period. The individual scatter of data increases much more when performing tasks with the left hand than with the right, and it is normalized by the 11th-21st days of adaptation (after the 3d day for the right hand), which is apparently also indicative of change in functional asymmetry of the hemispheres.

Tables 2 and 3 show the changes in LM and process of memorizing words. During adaptation to different conditions, the changes in LM are different: deferred reproduction and recognition become poorer after the transmeridional flight, whereas a tendency toward improvement of LM at the end of the observation period is observed with acclimatization to an altitude of 2500 m. During the adaptation period, fewer tests are required for stable memorization of the same volume of material than in the control. When memorizing material, there is also improvement of SM in the first reproduction, i.e., the results obtained with the other methods are confirmed (see Table 1).

We studied forgetfulness, reminiscence and interference on the same days. We found that there is less marked forgetting of words, particularly on the first few days: after the 4th day there was an increase in instances of reminiscence in the group (from 10 to 69%, Altay) and reliable increase in mean group level of reminiscence.

Proactive and retroactive interference decreased from the 4th day on during adaptation to an altitude of 2500 m and after the transmeridional flight. On the first few days, however, the process of change in PA and RA was unstable. By the end of the observation period, the values of RA were close to control levels, while the values of PA remained below the control.

The above results may also be of practical value in selecting the optimum mental work load when man spends time at high altitudes or after transmeridional flights.

BIBLIOGRAPHY

1. Aliyev, M. A. in "Fiziologiya i patologiya adaptatsiy k prirodnym faktoram sredy" [Physiology and Pathology of Adaptation to Natural Environmental Factors], Frunze, 1977, pp 98-100.

2. Il'yuchenok, R. Yu. "Pharmacology of Behavior and Memory," Novosibirsk, 1972; "Neurochemical Mechanisms of the Brain and Memory," edited by R. Yu. Il'yuchenok, Novosibirsk, 1977.

3. Slonim, A. D. "The Environment and Behavior. Formation of Adaptive Behavior," Leningrad, 1976.

4. Il'yuchenok, R. Yu. in "Fiziologiya i patologiya adaptatsiy k prirodnym faktoram sredy," Frunze, 1977, pp 42-44.

5. Bekhtereva, N. P. "Neurophysiological Aspects of Human Mental Activity," Leningrad, 2d edition, 1974.

6. Fraisse, P., and Piaget, J. (editors and compilers) "Experimental Psychology," Moscow, 1973.

7. Glass, G., and Stanley, G. "Statistical Methods in Pedagogics and Psychology," Moscow, 1976, p 279.

8. Sepetliyev, D. A. "Statistical Methods in Scientific Medical Research," Moscow, 1968, p 152.

9. Mirrakhimov, M. M.; Solozhenkin, V. V.; Shelukhina, E. P.; et al. in "Chelovek i sreda" [Man and the Environmnt], Leningrad, 1975, pp 59-70.

10. Baru, A. V. in "Sensornyye sistemy" [Sensory Systems], Leningrad, 1977, pp 85-114.

UDC: 613.693-07:612.825.2-056.172/.173

THE ROLE OF FUNCTIONAL ASYMMETRY OF THE CENTRAL NERVOUS SYSTEM IN PILOT PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 41-45

[Article by A. A. Gyurdzhian and A. G. Fedoruk, submitted 4 Jun 79]

[English abstract from source]

The paper describes a correlation between pilot performance and functional asymmetry of brain hemispheres. The correlation indicates that the pilots performing their flights uneventfully show higher indices of predominance of the left hemisphere (speach perception) and the right hand as compared to the pilots who perform their flights unsuccessfully and who have cardiovascular and nervous disorders.

[Text] One finds vivid examples of incidents related to pilot confusion of the right and left sides and, apparently, overt or discrete left-handedness in the scientific and nonscientific literature, as well as in practical flight work [1, 2].

A number of specialists studied the correlation between mancinism in pilots and the quality of their performance [3-7]. Specialists of the Norwegian Air Force [4] found that 31.6% of the pilots involved in flight incidents or near misses were left-handed, whereas manicism constituted only 7.6% of all pilots. The Scandinavian SAS Airline takes into consideration appropriate recommendations in this regard when screening flight personnel.

On the basis of data referable to the English Air Force, Gedye [3] showed that the share of left-handed individuals decreases constantly in the course of training and flight work because they drop out, since it was established that the professional qualities of such individuals are poorer.

It is known that asymmetrical sensitivity of the analyzers (both receptors and their central ends) and, primarily, the vestibular analyzer may serve as one of the important conditions for impairment of spatial orientation of a pilot, especially under difficult stressful conditions [8, 9].

At the same time, in spite of the correlation between lateralization of motor functions (right-handedness--left-handedness) and quality of pilot performance, there are quite a few excellent left-handed pilots. The lateralization of functions manifested in pilots constitute a complex blend of innate qualities and acquired skills. One can detect many transitional steps from right-handedness through so-called ambilaterality (ambidexterity) to left-handedness.

Evidently, one must search for finer and more graphic criteria of functional asymmetry of the central nervous system and their correlation to flying capacity. Experimental and clinical neuropsychology has a large number of observations pertaining to motor, sensory and psychoemotional symptoms in patients with lesions to one of the cerebral hemispheres. There are a number of methods of determining the nature and degree of dominance of one of the hemispheres. On this basis, in particular, diagnostics and therapy of various forms of agnosia and apraxia, including aphasia, are formed [10-13]. The problem of paired function of the hemispheres is the subject of basic research by Soviet physiologists and psychologists [14, 15].

The distinctions of lateralization of functions and concomitant function of the cerebral hemispheres are manifested (in addition to right-handedness and left-handedness) in such higher forms of mental activity as voluntary movement, concentration of attention, sensation of space and time [13, 15]. It is known that the left hemisphere is mainly specialized for analytical, abstract-symbolic activity on a verbal and sign [symbolic] basis, and performance of complex volitional acts, whereas the functions of the right hemisphere are characterized mainly by concrete, image-related thinking on a time and space basis, and they are of decisive significance in organizing human emotions, recognition and discrimination of nonverbal information.

Our objective here was to study the correlation between quality of professional performance of flight personnel and distinctions of functional asymmetry of the central nervous system.

Methods

We used the method of dichotic listening to words and a set of motor tests, which involved simultaneous delivery of different verbal stimuli (monosyllabic words) to both ears in order to determine which was dominant, for demonstration of individual distinctions of lateralization of functions, i.e., functional dominance of one of the cerebral hemispheres. We used 10-12 different motor tests (dynamometry, arm length, various tests involving work operations to be performed with both hands) and the subjects' history to assess the functional dominance of the right or left hand. In addition, we conducted tests to determine which was the dominant eye (aiming) and subjective estimation of time.

On the basis of the obtained data, determination was made of the following: index of dominance of the left hemisphere for speech perception (ratio of difference in number of words perceived by the right and left ear to the total number of verbal stimuli, %); index of dominance of the right hand (ratio of difference in number of tests with prevalence of right and left hand to number of tests in which dominance of one hand was noted, %).

We assessed flight performance on the basis of the service record, as well as the pilot's subjective report on professional difficulties, frequency and nature of experienced illusions referable to spatial position of the body. The physical condition of a pilot was assessed on the basis of the findings of outpatient and in-hospital examinations.

We studied three groups of pilots and cadets [students] with flight work tenure of 2 to 15 years, with total flying time of 80 to 200 h for the cadets and 300-1400 h for the pilots. The first group consisted of healthy pilots and cadets who performed flights well and had no accidents or near misses [preconditions for flight incidents] (37 pilots and 15 students); the second group consists of pilots (27 people) who had had accidents or near misses, and students (37) who were behind in their flight training. Following accidents and near misses, the pilots were examined every 6 months for up to 3 years. The third group consisted of 24 pilots mostly with functional diseases of the central nervous and cardiovascular systems. None of the subjects was over 30 years old.

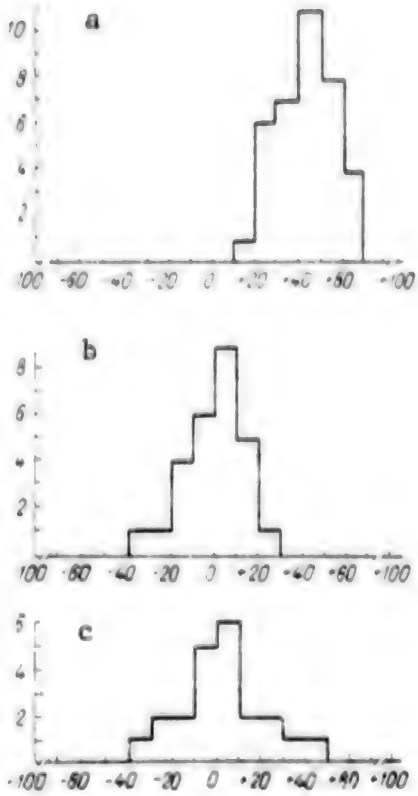
Results and Discussion

The index of functional dominance of the left hemisphere for speech perception was substantially higher in the first group (44.3% for pilots and 32.5% for students) than the second (11.8 and 14.2%, respectively (see Figure).

In the vast majority of pilots in the first group, the index of dominance was in the range of +20 to +60% without exceeding its boundaries (+10 to 70%, top histogram). In the second group of pilots, the index of dominance was chiefly in the range of +20 to -20%, occasionally reaching the limit (+30 -- -40%, middle histogram). Negative values for the index are indicative of dominance of the right hemisphere. Comparable asymmetry was observed in the corresponding groups of cadets.

The index of dominance of the right hand was also substantially higher in the first group than the second, constituting 67 and 31%, respectively. Overt and latent left-handed subjects were demonstrated only in the second group of pilots and students.

Some interesting results were obtained on the third group of subjects (bottom histogram). Their index of dominance of the left hemisphere for speech perception ranged essentially from +30 to -30%, sometimes reaching limits of +50 to -40%. The pilots in the third group were quite similar to those in the second group with regard to index of dominance of the left hemisphere (for speech perception).



Distribution of flight personnel as a function of index of dominance of cerebral hemispheres for speech perception. X-axis, index of dominance of cerebral hemispheres; y-axis, number of subjects

a) pilots who performed well and showed no deviations in health status
b) pilots who had accidents and near misses
c) pilots with functional diseases of the central nervous system and cardiovascular system

The question of correlation between features of functional asymmetry of the cerebral cortex (insufficient dominance of left hemisphere) and functional diseases of the central nervous and cardiovascular system of pilots in this group requires special investigation. There are indications that compensated elements of functional asymmetry (lateralization of functions) could be manifested, first of all, in the presence of stress, fatigue and illness [5-7]. On the other hand, expressly these features of asymmetry, which create considerable difficulties in flying, may serve as the prerequisites for disease. It is probably for this reason that it was often difficult to distribute pilots in the second and third groups: most of the "accident-prone" ones suffered from functional diseases, and many of those who were sick created potential incident situations. Some pilots themselves requested transfers to simpler aircraft equipment due to piloting difficulties; others were sent to a hospital for examination due to their physical condition or because of consistent mistakes in piloting.

Examples

1. Pilot M. He often experienced illusions of spatial body position, difficulties in flying in formation (particularly when banking) and fatigue of the right hand during his flights. In the hospital the diagnosis of neurocircular dystonia of the hypertensive type was made. He failed to demonstrate disturbances referable to the vestibular system.

His index of dominance of cerebral hemispheres for speech perception was -19%, which is indicative of dominance of the right hemisphere. The index of hand dominance was -18% (dominance of left hand). He considers himself to be left-handed. His right eye is dominant.

2. Pilot A. experienced considerable difficulties during flights, especially under poor meteorological conditions. Breaks away from flight work had a severe effect on the quality of his piloting technique. New types of flights were learned with difficulty. He made mistakes in piloting technique bordering on conditions for a potential flight incident. The index of dominance of the left hemisphere was +12% for speech perception and index of dominance of the right hand was 0, which is indicative of ambiexterity. The left eye is dominant. When examined at the hospital, the diagnosis of duodenal ulcer and vegetative emotional instability was made.

Thus, there was a correlation between quality of flying performance and distinctions of functional asymmetry of the cerebral hemispheres which, in our opinion, may be of theoretical interest and practical significance in medical certification for flight fitness and screening.

BIBLIOGRAPHY

1. DeSaint Exupery, A. "Wind, Sand and Stars," New York, 1944, p 190.

2. Beaty, D. "The Human Factor in Aircraft Accidents," London, 1969, pp 152-160.

3. Gedye, I. L. AEROSPACE MED., Vol 35, 1964, pp 757-763.

4. Gerhardt, R. in "Medical Aspects of Flight Safety," London, 1959, pp 262-272.

5. Rehberg, G. Z. MILITARMED., Vol 9, 1968, pp 108-112.

6. Idem, Ibid, Vol 12, 1971, pp 143-146.

7. Rehberg, G.; Peper, E.; and Schur, W. Ibid, Vol 10, 1969, pp 408-413.

8. Aschan, G. ACTA OTO-LARYNG. (Stockholm), Suppl 116, 1954, pp 24-31.

9. Caporale, R., and Camarada, V. RIV. MED. AERONAUT., Vol 21, 1958, pp 12-36.

10. Kok, Ye. P. "Visual Agnosia," Leningrad, 1967.

11. Mosidze, V. M., and Akbardiya, K. K. "Functional Symmetry and Asymmetry of the Cerebral Hemispheres," Tbilisi, 1973.

12. Luriya, A. R. "Higher Cortical Functions in Man, and Impairment Thereof in the Presence of Local Brain Lesions," Moscow, 1962.

13. Dobrokhotova, T. A., and Bragina, N. N. "Functional Asymmetry and Psychopathology of Focal Brain Lesions," Moscow, 1977.

14. Anan'yev, B. G. in "Problemy vospriyatiya prostranstva i prostranstvennykh predstavleniy" [Problems of Spatial Perception and Spatial Conceptions], Moscow, 19[illegible], pp 5-10.

15. Simernitskaya, E. G. "Dominance of the Hemispheres," Moscow, 1978.

UDC: 629.78+613.693]-07:612-763

DISTINCTIONS OF PILOT MOTOR ACTIVITY IN DIFFERENT PILOTING MODES DURING LANDING APPROACHES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 45-48

[Article by R. I. Brusnichkina, submitted 2 Jun 79]

[English abstract from source]

Complex motor acts of pilots during their professional work were investigated with control information presented in a different manner. Two experimental series were run in a real flight and in a simulator. Parameters of muscle bioelectric activity, control movements and performance efficiency were used. Differences in the formation of motor acts were shown to depend on the scope and quality of the information presented. During required transfer from one mode to another the structure of working movements and performance efficiency obeyed at large changes in the information necessary for piloting. This was accompanied by an alteration in the developed stereotype of actions, including motor acts.

[Text] The structure of the motor act is determined by central mechanisms that integrate the entire aggregate of afferent and intracentral influences and interactions [1, 2]. When performing tasks of the tracking type, the characteristics of the visual input signal are important to preparation of the program and formation of actions [3-5]. A change in presentation of information may be associated with a change in controlling movements and changes in the electromyogram (EMG) of functional muscles. Information displayed on the instrument panel is the basis for construction of a pilot's (astronaut's) controlling movements. Our objective here was to study the changes in motor activity and EMG of a pilot when such information is displayed in different ways.

Methods

Studies were pursued in the course of actual flights aboard the IL-18 aircraft laboratory and on a simulator. We examined the motor activity of a pilot while controlling an aircraft according to a flight director [guidance instrument](first mode), several instruments yielding uncoordinated information (second mode), with partial (transitory mode 3) and total (transitory

mode 4) elimination of guidance information. Pilot performance was examined during a landing approach with flight over a remote (RHS) and near (NHS) homing stations to an altitude of 30 m. A total of 29 pilots participated in this study. They made a total of 206 landing approaches in real flights and 272 on a simulator. A malfunction was created in the guidance system during 92 landing approaches in real flights and 96 on the simulator. The pilot had to change on his own, or upon being given a recommendation to do so, to a different piloting mode to complete the flight. We recorded the EMG of the group of hand and digital extensors of the right hand and angular deviations of the control surfaces in the lateral and longitudinal channels. We analyzed overall area under the EMG curve and signals of control deviations over the entire period of making the approach, dynamics of the integral EMG calculated for 30-s periods, as well as the time parameters of motor actions performed by the pilot. We used the mean quadratic deviations of heading (ΔE_h) and glide path (ΔE_{gl}) as indicators of efficiency of performance.

Results and Discussion

The visual pattern of the EMG, as well as its numerical characteristics, differed in accordance with the informational mode of work (see Table).

Changes in EMG, motor activity and efficiency of performance in the tested piloting modes, arbitrary units (M±m)

Mode	Area under EMG curve	Deviation of control surfaces	Efficiency index	
			ΔE_h	ΔE_{gl}
1	214±17.1	4.71±0.011	18.6±0.071	24.5±0.16
2	272±19.1	4.89±0.014	23.4±0.094	38.9±0.25
3 transition	221±13.7	5.36±0.018	22.0±0.111	30.2±0.27
after trans.	220±12.8	5.45±0.024	22.0±0.097	29.8±0.19
4 transition	290±16.5	5.93±0.021	29.7±0.150	47.6±0.34
after trans.	288±17.1	5.91±0.023	29.5±0.109	46.3±0.37

This table shows that the mean area under the EMG curve is substantially larger when piloting in mode 2 than in mode 1 (the differences are reliable with $P<0.05$). In the case of uncoordinated presentation of information, there is also decrease in efficiency of piloting, as manifested by increased deviations of heading and glide path. At the same time, the mean deviations of controls [rudders] in modes 1 and 2 do not differ from one another. In view of the fact that the physical exertion applied by the pilot to the control stick also failed to differ in the tested modes, it

may be assumed that the increase in area under the EMG curve reflects the complexity of the motor task itself. Evidently, the changes in EMG of forearm muscles are not so much related to the dynamic component reflecting the energy aspect of movement as it is to complex static tension of muscles, which is required for fine and precise coordination of the motor act. Afferentation from muscular tension serves as the basis for maintaining excitability of motor centers [6]. Perhaps, the differences in muscular tension reflect basic changes in nature of construction of movement and formation of a single motor act when information is presented in different ways. Figure 1 shows that the time of intervention in control with changes in main flight parameters (deviations of banking and pitching) changes substantially, depending on the control mode. In mode 2, the values of t_1 and t_2 are greater than in the case of delivery of command information. This time parameter, other conditions being equal, can characterize the process of formation of the program of movement, including the stage of its sensory organization.

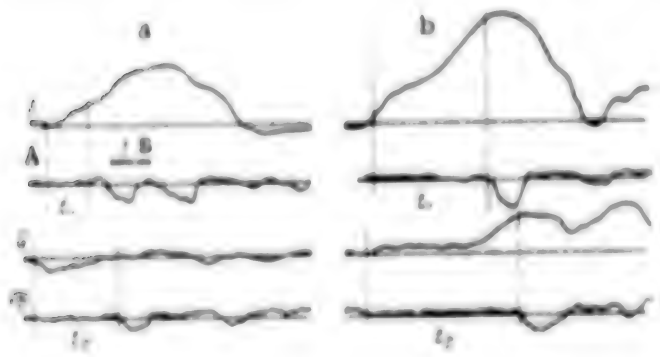


Figure 1.
Curves characterizing the time parameters of a single motor action as related to presentation of information (a--mode 1, b--mode 2).
t_1) time from start of banking (γ) to movement of ailerons (A)
t_2) time from start of pitching deviation (Q) to movement of elevator (PB)

The data in the Table are also indicative of substantial differences in piloting activity in modes 3 and 4. In mode 3, when the use of a properly functioning channel of command information is retained, the EMG parameters are lower and there are less marked deviations of heading and glide path than in mode 4. Thus, according to the overall changes in EMG and efficiency indicators, the difficulty of changing to another piloting mode is determined by the degree to which the information model is preserved. There is also a change in efficiency of performance, depending on the difficulty of the transition.

In addition to overall area under the EMG curve, we analyzed the dynamics of integral values over 30-s periods. The EMG signal recorded on tape was inputted in a computer, and calculation was made of the integral every 30 s for 2 min (which corresponded to mean landing approach time).* The first

*A. S. Kuz'min prepared the program for automatic processing of the EMG.

30 s of the EMG tracing characterized piloting in the normal mode. Modes 3 and 4 began after flying over the RHS, when a signaled malfunction of the flight director system was introduced. The duration of the transitional process was considered to be 30 s. We then examined 30-s periods of stable quality of piloting before and after flying over the NRS (Figure 2). A comparison of Figure 2a and 2b shows that, along with increase in EMG integral in mode 4, there is leveling off of its fluctuations, which is apparently indicative of higher tension of control mechanisms of the central nervous system. In mode 3, when the possibility of using part of the command information is retained, there are less marked changes in the 30-s EMG integral. This conclusion confirms with other observations of a link between the means of formation of movement and presentation of a control signal, as well as change therein in the course of tracking [3-5]. It is believed that mechanisms of motor memory are involved in programming movement, which include the programs of separate movements in the form of an orderly list of effector elements in a closed reflex ring [1, 7]. It may be assumed that formation of a movement with two types of information (in this case, integral and uncoordinated) occurs according to different motor programs, the appearance of which is determined at the sensory stage of the motor task. Probably, when making an abrupt change from one control mode to another there must be synthesis of some new motor program, or use of several simultaneously functioning muscle control systems. This leads to certain changes in motor behavior, and it is associated with EMG changes.

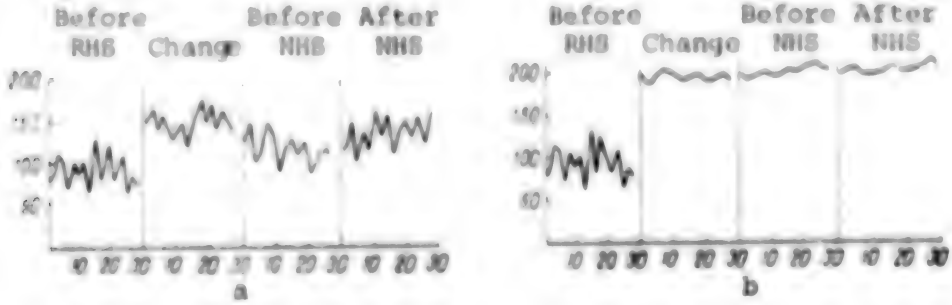


Figure 2. Changes in 30-s EMG integral when changing from one mode of control to another. X-axis, time (s); y-axis, EMG (arbitrary units)

a) change to control with partial use of guidance [command] information (from mode 1 to mode 3)
b) change to use of uncoordinated information from different instruments (from mode 1 to mode 4)

Thus, analysis of the EMG, along with amplitude and time characteristics of control movements, enables us to undertake an objective evaluation of motor systems and determine the degree of retention or impairment of piloting skills with change in amount of necessary information and means of presenting it.

BIBLIOGRAPHY

1. Bernshteyn, N. A. VOPR. PSIKHOL. [Problems of Psychology], No 6, 1957, p 70.

2. Person, R. S. "Electromyography in Studies of Man," Moscow, 1969.

3. Berezhnaya, O. K., and Rokotova, N. A. in "Mezhdunarodnyy simpozium 'Pererabotka zritel'noy informatsii i regulyatsiya dvigatel'noy deyatel'nosti'" [International Symposium on "Processing of Visual Information and Regulation of Motor Activity"], proceedings, Sofia, 1971, p 539.

4. Lyubomirskiy, L. Ye. "Control of Movements in Children and Adolescents," Moscow, 1974.

5. Rokotova, N. A. in "Sensornaya organizatsiya dvizheniy" [Sensory Organization of Movements], Leningrad, 1975, pp 174-180.

6. Ukhtomskiy, A. A. "Collected Works," Leningrad, Vol 3, 1950.

7. Batuyev, A. S. in "Sensornaya organizatsiya dvizheniy," Leningrad, 1975, pp 23-31.

UDC: 612.176.4.014.477-063

EFFECT OF PERIODIC EXPOSURE TO 'HEAD-PELVIS' ACCELERATIONS ON A SHORT-ARM CENTRIFUGE ON RESPONSES OF THE HUMAN CARDIOVASCULAR SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 48-51

[Article by I. F. Vil'-Vil'yams, submitted 17 Aug 78]

[English abstract from source]

During 3- and 6-day immersion studies test subjects were two or three times a day (60 min each time) exposed to head-to-feet acceleration of 1-2 G in a 2 m arm centrifuge. In 297 runs cardiovascular reactions were compared with respect to their adaptation or cumulation. The results obtained showed that the principle of periodic application of acceleration in a short-arm centrifuge as a countermeasure against cardiovascular deconditioning can be complemented by the principle of cyclic exposures. The study demonstrated that 3-day cycles including 60 min exposures to 1-2 G, twice a day were most efficient.

[Text] Low level accelerations on an onboard short-arm centrifuge (SAC) are one of the possible means of preventing the adverse effects of weightlessness during long-term space flights [1, 2]. However, in the literature available to us we did not encounter information concerning evaluation of adaptation and cumulative effects of using different variants of periodic rotation on an SAC.

Our objective here was to compare the reactions of the human cardiovascular system to 3- and 6-day preventive cycles of periodic exposure to "head-pelvis" accelerations on an SAC in the range of +1-2 G.

Methods

A total of 297 tests on 16 health male volunteers was conducted on an SAC (arm length 2 m). The axis of rotation passed on the level of the eyes through the region of the bridge of the nose. The tests were conducted under conditions simulating the effects of deconditioning of the body by means of "dry" submersion in an immersion medium, with the use of hyperelastic waterproof fabric [5].

In the first series of tests (96 observations), we studied the effects of accelerations of 0.8, 1.2 and 1.6 G (at the level of the feet) lasting 60 min. Studies were made twice a day for 3 days. The resulting accelerations constituted 1.3, 1.6 and 1.9 G, respectively. In the second series (158 cases), we tested the effect of accelerations of analogous levels lasting 40 min. We examined the subjects 3 times a day for 3 days. In the third series (48 cases), the subjects were exposed to 0.8 G accelerations for the first 2 days, 1.2 G for the next 2 days and 1.6 G for the last 2 days. Duration of each exposure was 60 min and frequency was twice a day. The intervals between exposures in the latter cases constituted 10 and 12 h, and in the case of 3-fold exposure, 6.6 and 9 h. Each subject was rotated for a total of 6 times in the first series of tests, 9 times in the second and 12 times in the third.

During all of the tests, we recorded the electrocardiogram in the Neb leads; in the second and third series we took photoplethysmograms (PPG) of the first toe using a sensory manufactured by the Japanese firm of Nihon Kohden; in the third series we measured arterial pressure (AP) in vessels of the leg by the tachooscillographic method [6] using an AD-KTs Biofizpribor instrument. The range of pressure readings was 200 mm Hg. We calculated the heart rate (HR), PPG amplitude for the first toe and minimum AP in leg vessels every 5-10 min of rotation on the SAC. Then, using these data, we determined the mean values of the parameters studied for the plateau. In order to obtain integral values of parameters characterizing each day of the study, we added all of the mean values thereof per plateau for each day of the study, and we divided the sum by the number of rotations per day. We visually examined the integument of the legs and feet for hemorrhages before and after exposure to accelerations.

The data were processed by the Student method of variational statistics. The differences were considered reliable with $P<0.05$.

Results and Discussion

In the first series of tests with accelerations of 1.2 and 1.6 G_z, overall values for the HR on the 2d and 3d days did not change appreciably, as compared to the first day (Figure 1). With acceleration of 0.8 G, there was a tendency ($P<0.2$) toward decline of HR on the 3d day, as compared to the 2d.

In the second series, with accelerations of 1.2 and 1.6 G, we observed a statistically reliable ($P<0.05$) build-up of sinus tachycardia on the 2d and 3d days of the tests. With acceleration of 0.8 G, there was a marked tendency ($P<0.1$) toward increase of HR on the 3d day, as compared to the 1st. The amplitude of the PPG of the first toe diminished in some subjects with accelerations of 1.2 and 1.6 G on the 3d day, as compared to the 1st, although this difference was not statistically significant for the group as a whole. Visual examination of the integument of the legs and feet revealed petechial hemorrhages after termination of the test in one subject. During rotation, appearance thereof was preceded by a drop almost to the base line in amplitude of PPG of the first toe.

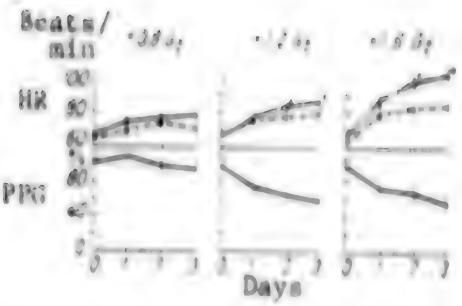


Figure 1.
Dynamics of cumulative values of parameters of cardiovascular system from 1st to 3d days of exposure to accelerations of +0.8, 1.2 and 1.6 G_z on an SAC 2 and 3 times a day during immersion. Solid line--values of parameters with 3-fold rotation, dash line, with 2-fold rotation. Here and in Figure 2, asterisk shows $P<0.05$ (as compared to 1st day)

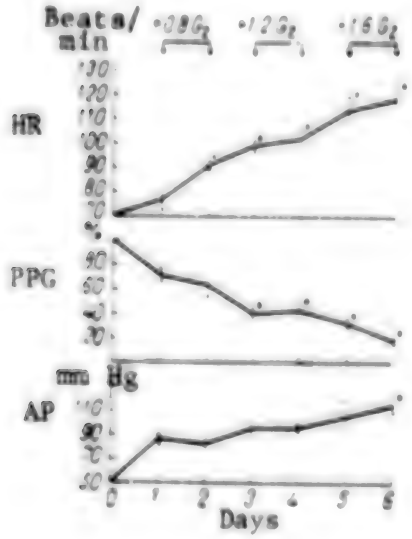


Figure 2.
Dynamics of cumulative values of parameters of cardiovascular system from 1st to 6th days of exposure to 0.8, 1.2 and 1.6 G_z in a progressive mode on SAC, twice a day, with immersion

In the third series of tests with repeated exposure to accelerations in a progressively increasing mode, we observed a reliable ($P<0.05$) increase of HR, decrease in amplitude of PPG of the first toe and significant elevation of minimum AP of leg vessels (Figure 2). The changes in the parameters studied in the course of the 6-day cycle were essentially determined by the increase in accelerations every 2 days. In some cases, we also found reliable increase in changes referable to the cardiovascular system with exposure to accelerations of the same magnitude. Thus, with 1.6 G, we observed a substantial decrease in amplitude of PPG of the first toe on the 6th day, as compared to the 5th. Visual examination of the integument of the legs and feet after repeated exposure to accelerations in the course of the 6-day cycle revealed petechial hemorrhages in all subjects.

Analysis of the changes in cardiovascular system parameters on the last day of the test and comparison thereof to base values ($\Delta\%$) showed that the changes in parameters studied with accelerations of 1.6 G were more marked in the 6-day cycle than the 3-day one. Thus, on the last day of the 6-day cycle, HR increased by 63%, versus 35 and 54% in the first and second series of tests, respectively, where 3-day cycles were used. Within an analogous period of time, the amplitude of the PPG of the first toe decreased by a mean of 81% in the 6-day cycle and by a mean of 44% with the 3-day cycle in the second series.

As we see from the foregoing, periodic exposure to accelerations of low magnitude (1-2 G) may elicit adaptive and cumulative (deleterious) effects. For example, the increase in intensity of function of the

cardiovascular system in the first series of tests can be evaluated as a manifestation of processes of adaptation to accelerations. The progressive build-up of changes in physiological parameters and appearance of hemorrhages in the second and third series are indicative of accumulation of adverse effects of accelerations.

It is known that development of adaptation or cumulative effects of numerous exposures to accelerations is determined by their direction, magnitude, duration, frequency of repetition, intervals between exposures and initial functional state of the body [7, 8]. In this regard, it can be assumed that the appearance of cumulative effects in the second and third series, and absence thereof in the first series, with the same magnitude of accelerations was due to the higher frequency of exposures. A comparison of the results of the first and second series leads us to the conclusion that the functional state of the cardiovascular system also depended on the length of the intervals between exposures to accelerations.

Analysis of our data and comparison thereof to the literature [9-12] revealed that the chronotropic reaction of the heart and the parameters characterizing regional circulation in the lower extremities are informative physiological parameters that permit evaluation of adaptation and cumulative effects.

The progressive decline in amplitude of the PPG of the first toe and elevation of minimal AP in leg vessels are indicative of the presence of arterial vasoconstriction in the lower limbs and marked increase in peripheral vascular resistance [6, 12, 13].

The obtained facts characterizing the reactions of the cardiovascular system as related to various many-day cycles of periodic exposure to "head-pelvis" acceleration on an SAC in the range of 1-2 G could serve as the basis for choosing an optimum variant for using an onboard centrifuge. Development of cumulative effects with frequent (3 times a day) exposure to accelerations indicates that it is not desirable to use continuous rotations on an SAC. Among the tested many-day cycles of periodic exposure to accelerations in the range of 1-2 G, the optimum ones, i.e., those that did not elicit cumulative effects, were the 3-day cycles used twice a day. Since it is impossible to simulate accelerations with a resultant of under 1 G on the ground, one must make the final determination of parameters of rotation on an onbaord centrifuge, as a means of preventing the adverse effects of weightlessness, under actual space flight conditions.

BIBLIOGRAPHY

1. White, W. J. in "Symposium on the Role of the Vestibular Organs in the Exploration of Space," 1st, Proceedings, Washington, 1965, pp 209-213.

2. Burnazyan, A. I.; Vorob'yev, Ye. I.; Gazenko, O. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1977, pp 3-12.

3. Shul'zhenko, Ye. B. "Physiological Effects of Altered Gravity (Ground-Based Model Experiments)," doctoral dissertation, Moscow, 1975.

4. Kotovskaya, A. R.; Galle, R. R.; and Shipov, A. A. KOSMICHESKAYA BIOL., No 2, 1977, pp 12-19.

5. Shul'zhenko, Ye. B., and Vil'-Vil'yams, I. F. Ibid, No 2, 1976, pp 82-84.

6. Savitskiy, N. N. "Some Methods of Studying and Making a Functional Evaluation of the Circulatory System," Leningrad, 1956.

7. Khazen, I. M.; Kogan, E. M.; and Barer, A. S. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, 1963, pp 469-472.

8. Stepantsov, V. I., and Yeremin, A. V. KOSMICHESKAYA BIOL., No 6, 1969, pp 47-54.

9. Jongbloed, J., and Moyons, A. K. PFLUG. ARCH. GES. PHYSIOL., Vol 233, 1933, pp 67-97.

10. Vasil'yev, P. V., and Kotovskaya, A. R. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 1, 1975, pp 177-231.

11. Barer, A. S. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 7, 1958, pp 56-59.

12. Folkov, B., and Nil, E. "Circulation," Moscow, 1976.

13. Wiggers, K. "Dynamics of Circulation," Moscow, 1957.

UDC: 629.78:612.766.2-08:611.984

EFFECT OF ANTIORTHOSTATIC HYPOKINESIA AND SPACE FLIGHT FACTORS ON CHANGE IN LEG VOLUME

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 51-55

[Article by I. I. Kas'yan, V. A. Talavrinov, V. I. Luk'yanchikov and Ye. A. Kobzev, submitted 7 Aug 79]

[English abstract from source]

The purpose of the present investigation was to assess, using a specially built sensor, variations and level of fluid redistribution as well as atrophic changes in leg muscles of test subjects exposed to prolonged head-down tilt and cosmonauts in a real space flight. Hypokinetic test subjects were examined before, during and after head-down tilt, whereas cosmonauts were examined before and during flight. The results obtained show that a change in the hydrostatic component of blood pressure is followed by displacement of a substantial fluid volume (about 7%). Adequate performance of pre-assigned countermeasures seems to prevent atrophic developments of leg muscles.

[Text] It has now been determined that redistribution of blood, which is unusual on earth, with increase in influx thereof to organs and parts of the body above the level of the heart, is one of the triggering factors in the reactions of alteration of the function of many systems of the body in real or simulated weightlessness [1-3].

However, not all aspects of gravitational redistribution of blood have been studied as yet. The first quantitative data characterizing the extent and dynamics of this process were obtained during the flights on the Skylab program [3, 4].

The decrease in volume of muscles of the limbs (mainly lower ones) is one of the factors of the effects of space flights on the human body. The information in the literature concerning the effects of different physical loads [exercise] used to prevent possible muscular disorders is contradictory [5-7].

We have tried to define, in assessement of leg volume (LV), the extent and dynamics of redistribution of body fluids and deconditioning of certain

muscle groups with change in magnitude of the hydrostatic component of arterial pressure during performance of exercises used for preventive purposes.

Methods

LV was determined by means of a specially developed measuring device. Tape measures situated over the elastic part of this device enabled us to evaluate perimeters on 8 levels 3 cm apart from one another. On the assumption that the segments contained between the tape measures are truncated cones, we determined the volume of a segment of the crus 24 cm in length as the sum of 7 truncated cones.

We examined 18 male volunteers in the course of 182-day antiorthostatic [head down] (-4.5° tilt) hypokinesia and two cosmonauts (crew members of the second main expedition) during a flight aboard the Salyut-6--Soyuz orbital research complex.

We determined LV in subjects submitted to hypokinesia in the morning, in "supine--legs extended" position during the background period (BP). on the 6th, 46th, 70th, 110th, 154th and 172d day of the study period, and on the 2d-5th, 33d and 53d days of the recovery period (RP).

All of the subjects were divided into three groups with six in each. To prevent any possible disorders, we used a set of measures in the first group, one element of which was physical exercise on a special exerciser [8]. The subjects in the second group performed a set of physical exercises that represented one-half the time and energy expended, as compared to the first group. No preventive measures were used with the individuals in the third (control) group.

We measured LV of cosmonauts concurrently, in the background period, on the 4th-11th, 22d, 82d, 97th, 102d, 111th and 120 days of the flight. In addition, we also measured it on the 31st, 38th, 40th and 55th flight days for the commander, on the 39th and 59th flight days for the flight engineer. It should be noted that the volume of physical exercise performed by the cosmonauts was close to the scheduled level.

The changes in LV (in relation to background values) were evaluated in all subjects in relative (%) and absolute (cm^3) figures. The results of the ground-based tests were submitted to statistical processing.

Results and Discussion

Analysis of the data obtained in the studies involving 182-day hypokinesia revealed that the rate of change in LV differed at different stages of hypokinesia.

Thus, there was relatively uniform decrease in LV in the third group up to the 70th day of hypokinesia. In this time it diminished by 11.5% ($P<0.05$). In the next 100 days, the LV in this group of subjects changed by only 0.8%.

In the second group, the changes in LV differed little from the dynamics in the third group up to the 46th day: in this time it diminished by 9.1%, then by 1.2% by the 70th day and by another 1.3% by the end of the study.

There was less decrease, by 5.9%, in LV in subjects of the first group by the 46th day; it decreased by another 1.6% within the next 14 days, and by 2.0% by the 172d day, which was somewhat more than in the third and second groups in the same period (last 14 weeks).

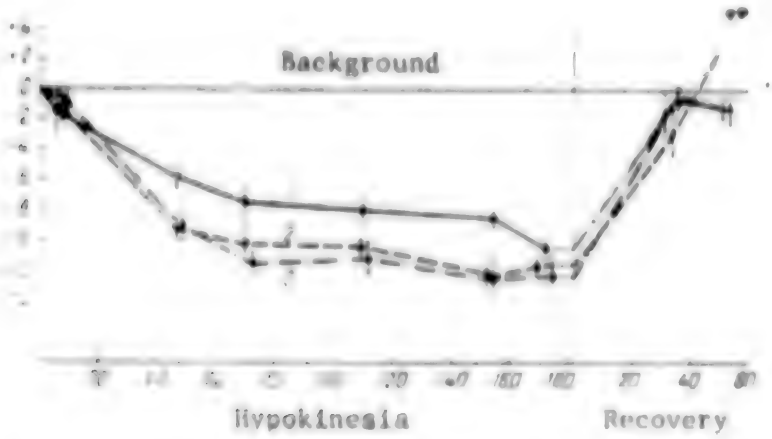


Figure 1. Dynamics of changes in leg volume of individuals kept under antiorthostatic hypokinetic conditions.
Here and in Figure 2: x-axis, days; y-axis, leg volume (% of background values). 1-3--1st, 2d and 3d groups of subjects, respectively.

The overall changes in LV were the greatest in the third group, constituting 12.3% (267 cm^3, $P<0.05$); they were somewhat less marked in the second group--11.6% (260 cm^3). This parameter constituted 9.5% (226 cm^3) in the first group.

The return of LV to the initial level also presented some distinctions (Figure 1): by the 2d-5th day of the RP it increased by 7% (this point is not illustrated on the curve, since only 8 individuals from different groups were examined). If we were to assume that LV changed to the same extent in the other 10 subjects, the increase in this parameter constituted 7% of all changes in the first group, 60% in the second and 57% in the third. By the 34th day of this period, this parameter was virtually the same as in the background, or else exceed the latter, in all groups (see Figure 1).

At the time of the first measurement in weightlessness (4th day), LV of both cosmonauts decreased by 6-7%. By the 11th day, the decrease in volume rose to 12% in the commander and 8% in the flight engineer. Thereafter, this parameter continued to decline, dropping by 16% in the commander and 14% in the flight engineer by the end of the 3d week, to 21-23 and 18-19%, respectively by the 82d-97th day of weightlessness. On the last 20 days of the observation period, there was no appreciable change in LV of either cosmonaut (Figure 2).

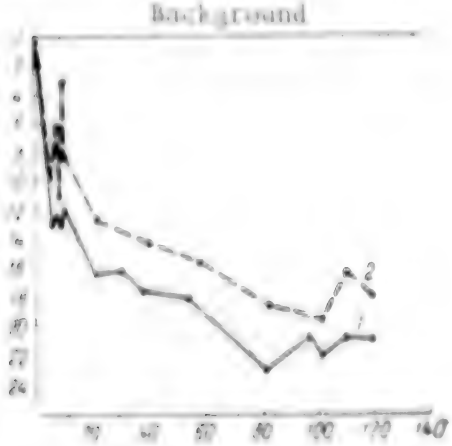


Figure 2.
Dynamics of changes in LV of crew members during second expedition aboard the Salyut-6--Soyuz orbital research complex
1) commander
2) flight engineer
Asterisk indicates that the measurement was taken after massaging the leg.

Thus, in the course of an actual flight, there was more appreciable decrease in LV of cosmonauts in the first 3 weeks of weightlessness. In the model study, the main patterns of change in this parameter were retained in the subjects. The perimeters on different levels decreased to different extents in the two groups. In all cases, they changed less appreciably in the upper third of the leg and more significantly in the region of maximum development of muscle tissue.

These data warrant the assumption that part of the loss of volume of lower extremities of individuals submitted to hypokinesia and of cosmonauts should be referable to fluid that shifted in a cranial direction and was then partially eliminated. Replacement of 7% of LV loss on the first few days of the RP in subjects submitted to hypokinesia and an analogous loss in cosmonauts during the acute period of adaptation to weightlessness are apparently due primarily to the effects of these factors.

Here then is different amounts of exercise affect the leg muscles? Performance of the regulation set of preventive measures not only prevented, almost entirely, development of atrophic processes in the first group of subjects (the difference between volumes after restoration of fluid balance constituted 1.7%), but aided in preserving their functional capacities on a high level.

Conversely, the substantial impairment of parameters of functional state of muscle tissue, along with appreciable (5.1%) decrease in LV during the acute readaptation period in subjects of the third group, is most probably related to development of the process of atrophy of the monitored muscle groups that are not sufficiently active. The same factors apparently

cause almost equally appreciable lack of recovery of LV (4.6%) in subjects of the second group.

The increase in weight of the subjects, associated with accumulation of adipose tissue (particularly in the third group) makes it probable that there is development of a process of replacement of part of the atrophied muscular tissue with fatty tissue, which obscures the loss of the main tissue and LV, as well as that there is equalization of the difference in these volumes in the second and third groups.

The absence of postflight tests makes it somewhat difficult to interpret the obtained data. However, the dynamics of recovery of body weight and perimeters of the thigh and leg, which, it is true, were measured on the same level, warrants the assumption that, in spite of adequate intake of fluid and food and the preventive measures, the deficient LV in the cosmonauts was attributable to both displacement of fluids and change in fluid balance of the body, as well as atrophic processes in muscle tissue.

A comparison of the data obtained from the ground-based and in-flight studies shows that the changes were more marked in the cosmonauts in the compared periods (6th, 39th-46th, 110th days). We were impressed by the more appreciable difference in rate of change in volumes in the two groups for the first few days of exposure to the different factors (0.4-1.6% in hypokinetic subjects and 6-7% in cosmonauts).

Thus, our findings confirm the theoretically substantiated hypothesis and information of other authors concerning the redistribution of fluid in weightlessness and head-down hypokinesia, and rapid recovery of the initial state upon returning to ordinary conditions. This displacement is apparently one of the mechanisms through which the human body adjusts to changing conditions within a short period of time.

BIBLIOGRAPHY

1. Gauer, O. H. in "Man in Space," Moscow, 1974, pp 176-193.

2. Kovalenko, Ye. A. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1976, pp 3-15.

3. Thornton, W. E.; Moffler, G. W.; and Rummel, J. A. in "Skylab Life Sciences Symposium," Proceedings, Houston, Vol 2, 1974, pp 211-237.

4. Whittle, M.; Herron, R.; and Cuzzi, J. Ibid, Vol 1, pp 413-423.

5. Pamov, A. G.; Ushzin, V. S.; and Belyankin, V. A. in "Problemy Kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 11, 1969, pp 131-141.

6. Tishler, V. A.; Anashkin, O. P.; Fervushin, V. I.; et al. In "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 190-192.

7. Thornton, W. E., and Rummel, M. D. in "Skylab Life Sciences Symposium," Proceedings, Houston, Vol 1, 1974, pp 401-414.

8. Kakurin, L. I.; Katkovskiy, B. S.; Tishler, V. A.; et al. KOSMICHESKAYA BIOL., No 3, 1978, pp 20-27.

UDC: 612.766.2

SOME OF THE PHYSIOLOGICAL EFFECTS OF 30-DAY BED REST WITH THE BODY IN DIFFERENT POSITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 55-58

[Article by B. S. Katkovskiy, V. S. Georgiyevskiy, G. V. Machinskiy, V. M. Mikhaylov and Yu. D. Pometov, submitted 7 Mar 79]

[English abstract from source]

Eighteen male test subjects were exposed to a 30-day bed rest with the head and [illegible] at +6°, -3° or -6°. Control subjects were allowed a normal motor activity during the same period of time. Hypokinesia was shown to play the leading role in the genesis of most changes while orthostasis appeared to support it. It was concluded that head-down tilt simulated changes occurring during adaptation to weightlessness better than recumbency or head-up tilt.

[Text] The antiorthostatic [head tilted down] model of weightlessness, which makes it possible to reproduce some of the physiological effects experienced by cosmonauts at the early stage of adaptation to weightlessness, was first used in our country [4-6]. The main objective of this work was to make a deeper study of the model of weightlessness by assessing the effect of the degree and direction of change in hydrostatic pressure (from +6 to -6° between the horizontal and longitudinal axis of the body) during strict bed rest. In addition, we had to determine whether the observed changes were the consequence of the numerous tests (orthostatic tests, physical loads [exercise], taking venous blood, etc.) that are usually conducted on healthy individuals in such studies.

Methods

A total of 24 male volunteers, ranging in age from 19 to 35 years, participated in this study; they were separated into 4 groups, with 6 men in each, according to anthropometric data, level of physical conditioning and orthostatic stability. For 30 days, the subjects in the first, second and third groups were kept on strict bed rest (BR) with the body in orthostatic (+6°) and antiorthostatic (-3 and -6°) positions. The fourth group of subjects (control) were not restricted in their movements, and they

lived under the same conditions, were on the same diet and submitted to analogous studies. They made up for the lack of activity that is inevitable in a hospital by performing a set of exercises.

In order to assess the condition of the subjects, in addition to general clinical tests and examination of respiration and circulation under basal metabolic conditions, we performed the following functional tests: 1) "passive" orthostatic test tilting the turntable to 85°, head up, for 20 min; 2) "graded" exercise for 5 min, constituting 600 kg-m/min, on a bicycle ergometer in "seated" position, starting with 600 kg-m/min in the first min and increasing in steps to 200 kg-m in the 2d and each subsequent min until the subject reported that he could no longer continue to pedal at the specified rate (65±6 r/min).

During the orthostatic test, we counted the heart rate (HR) on the EKG and determined pulse pressure (PP); in addition to HR, we determined oxygen uptake under basal metabolic conditions and while exercising, using an automatic gas analyzer, with calculation of oxygen [?] pulse (OP), as well as stroke volume (SV) of the heart (only at rest and with a load of 600 kg-m/min) by the method of CO_2 rebreathing [6].

Results and Discussion

The general condition of the subjects was satisfactory throughout the study period. The sensations experienced by subjects in the first to third groups at the start of BR were related to the angle of inclination of the bed. Those who were in orthostatic (+6°) position observed a feeling of "fever" in the legs and increased foot perspiration; they presented signs of increased delivery of blood to the feet and legs. The subjects who were in antiorthostatic position (-2 and -6°) experienced "fever" in the head and upper part of the trunk, with heaviness and "bloating" of the neck and head, stuffed nose and ears, cold legs. Objectively, they had a husky voice, presenting edema and hyperemia of the face.

The process of adaptation to the unusual conditions was associated with individual distinctions, and it lasted mostly up to the 15th day of hypokinesia. In the second half of the BR period, there was significant leveling off of the difference in clinical status of the subjects.

In the first three groups of subjects, there was an appreciable decrease in oxygen uptake under basal metabolic conditions, regardless of angle of tilting of the bed, while no substantial differences in gas exchange were observed in the fourth group. Under such conditions, SV increased on the very first days of BR in individuals who were in antiorthostatic positions (-2 and -6°), whereas it did not change appreciably in the first half of the BR period in subjects in orthostatic position (+6°).

Some hemodynamic and gas exchange parameters of subjects in different groups before start and after end of 30-day BR, at rest and during performance (5th min) of exercise corresponding to 100 W, M±m

Group	Angle	Time of exam.	HR/min		SV, ml		CP, ml/beat	
			rest	exercise	rest	exercise	rest	exercise
1	[illegible]	Before BR	80±7.1	116±3.2	73±6.9	115±8.9	3.90±0.1	12.4±0.7
		After BR	98±7.3	137±5.6	43±11.8	94±3.9	2.88±0.2	10.2±0.5
			(+21.0)	(+18.1)	(−41.1)	(−18.3)	(−26.2)	(−17.9)
2	[illegible]	Before BR	80±2.8	118±4.4	63±6.7	117±3.8	3.84±0.2	12.5±0.5
		After BR	101±6.5	138±7.8	48±4.5	97±5.5	3.15±0.1	9.96±0.1
			(+26.0)	(+16.9)	(−23.8)	(−17.1)	(−18.0)	(−19.2)
3	6°	Before BR	73±6.9	114±[illegible]	74±5.6	122±5.1	4.23±0.3	12.4±0.3
		After BR	101±9.0	145±2.5	58±3.3	102±4.0	2.76±0.3	9.7±0.3
			(+38.4)	(+27.2)	(−21.6)	(−16.4)	(−34.8)	(−21.8)
4	Control	Before BR	89±3.4	122±4.7	70±9.0	109±7.1	3.8±0.1	12.0±0.4
		After BR	79±3.9	117±6.2	80±7.2	134±4.8	4.0±0.1	12.3±0.9
			(−11.2)	(−4.1)	(+14.3)	(+22.9)	(+5.2)	(+2.5)

After the BR period, there was substantial deterioration of endurance of orthostatic and physical loads in the first to third groups of subjects, as compared to base data; after the 30-day observation period, there was virtually no change in endurance of these factors in subjects of the fourth group. A statistically significant ($P<0.05$) intergroup difference in change of most parameters recorded was observed only between the fourth and the other groups.

During the orthostatic tests performed after BR, there were two cases of syncope in the first group, 4 in the second and 2 in the third, whereas no syncopes had been recorded prior to BR. The reaction of the cardiovascular system to this test worsened drastically in the first to third groups of subjects: increased HR and decreased PP (Figure 1).

In the tests with moderate physical loads (600 kg-m/min) after termination of BR, we observed marked changes in the parameters studied in the first to third groups of subjects, both at rest and during exercise, and they were indicative of poorer reactions of the cardiovascular and respiratory systems to these factors (see Table).

During the test with maximum physical load after termination of BR, we observed approximately the same mean decrease for the groups in pedaling time and decline of maximum oxygen uptake and OP in the first to third groups of subjects (Figure 2). Thus, the decline of parameters of fitness during the test with the maximum physical load after termination of BR was unrelated to the position of the body.

These studies demonstrated convincingly that performance of an extensive amount of clinical and physiological tests did not have an appreciable effect on

healthy individuals. This is confirmed by the good functional state of the subjects in the fourth group, which remained close to the initial condition throughout the study.

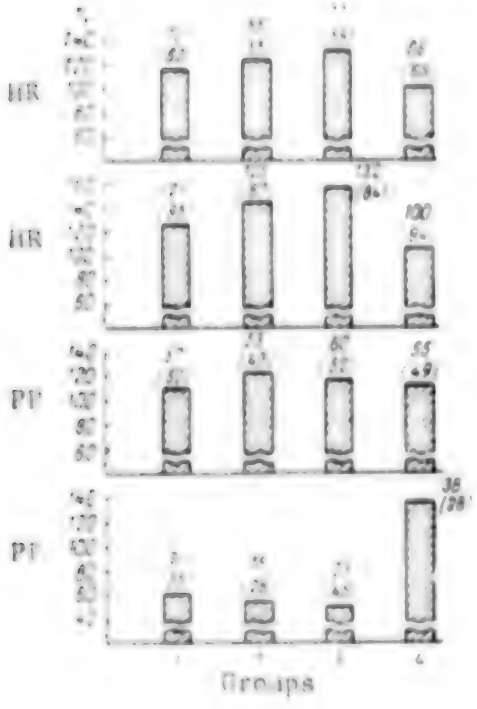


Figure 1.
Relative change (%) in HR and PP of subjects in different groups during orthostatic test after termination of 30-day bed rest (mean data)
Top to bottom: horizontal and vertical body position. Here and in Figure 2: numbers above columns are absolute values of HR (per min) and PP (mm Hg) before (in parentheses) and after BR

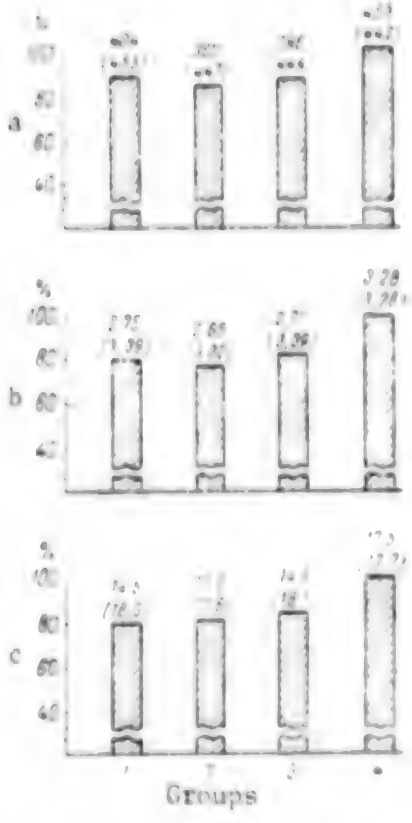


Figure 2.
Relative changes in exercise time (a, in seconds); maximum oxygen uptake (b, ℓ/min) and maximum OP (c, ml/beat) during test with maximum physical load; subjects in different groups, after 30-day BR (mean data)

The obtained data indicate that restricted muscular activity acquires the leading role in the genesis of most disturbances when duration of hypokinesia is increased to 30 days. The change in hydrostatic pressure and absence of hydrodynamic fluctuations (which usually occur when walking and running) can apparently cause development of circulatory disorders under these conditions. This is indicated, in particular, by the results of the studies, which showed that one cannot fully preserve orthostatic stability of individuals who spent 49 days in antiorthostatic position (-4.5°) by physical conditioning alone [7].

On the whole, the general phenomenology of disturbances observed in the first three groups of subjects was typical of hypokinesia of moderate duration. However, there were some intergroup differences from the very start of BR and immediately after termination thereof referable to clinical findings, which were determined by the distinctions of redistribution of blood in orthostatic or antiorthostatic position of the body. The phenomenology of disorders observed in individuals who were in antiorthostatic position (-6°) resembled in many respects the findings made in cosmonauts during the "acute" period of adaptation to weightlessness and readaptation to earth's gravity [1-3]. Very similar changes were also found in studies conducted for shorter periods of time with the use of antiorthostatic hypokinesia (up to -12°) as a model of weightlessness [8].

The results of this and previous studies [4-8], as compared to data obtained from examinations of cosmonauts, indicate that antiorthostatic hypokinesia is a more adequate model than BR with the body in horizontal or orthostatic position for the reproduction of different hemodynamic disorders that occur in the "acute" period of adaptation to weightlessness.

BIBLIOGRAPHY

1. Gazenko, O. G.; Kakurin, L. I.; and Kuznetsov, A. G. (editors) "Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniya" [Space Flights Aboard the Soyuz Series Spacecraft. Biomedical Studies], Moscow, 1976.

2. Gurovskiy, N. N.; Yeremin, A. V.; Gazenko, O. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1975, pp 48-54.

3. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. Ibid, No 5, 1976, pp 3-18.

4. Genin, A. M., and Kakurin, L. I. Ibid, No 4, 1972, pp 26-28.

5. Voskresenskiy, A. D.; Yegorov, B. B.; Pestov, I. D.; et al. Ibid, pp 28-32.

6. Pometov, Yu. D., and Katkovskiy, B. S. Ibid, pp 39-46.

7. Kakurin, L. I.; Katkovskiy, B. S.; Tishler, V. A.; et al. Ibid, No 3, 1978, pp 20-27.

8. Mikhaylov, V. M.; Alekseyeva, V. P.; Kuz'min, M. P.; et al. Ibid, No 1, 1979, pp 23-28.

UDC: 612.53.014.477-064"52"

CIRCADIAN RHYTHM OF HUMAN BODY TEMPERATURE IN ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 59-61

[Article by L. Lkhagva, submitted 13 Aug 79]

[English abstract from source]

Circadian rhythms of the oral temperature were studied in three male test subjects kept for 7 days in a head-down position at −8°. As compared to the controls (kept in a hospital for 3 days) the test subjects showed a statistically significant temperature increase (by 0.22°C on the average) during circadian minimum points that occurred at night and a decrease of the daily temperature rhythm amplitude (by 0.20° on the average). It is emphasized that study of human responses to various stress-agents should include monitoring of circadian rhythms of various parameters.

[Text] There has been a considerable increase in interest in the phenomenon of biological rhythms at the present time, and the advances in space exploration were largely instrumental in this [1-4].

Our objective here was to study the distinctions of the circadian rhythm of human body temperature in antiorthostatic [head-down] position, which simulates to some extent some of the effects of weightlessness [5-9].

Methods

We conducted this study in November and December at moderate altitudes (atmospheric pressure constituted a mean of 856.1 mbar over the entire study period). The participants were three healthy men 28-30 years of age who were permanent residents of the locality. At the main stage of the study, the subjects maintained bed rest (BR) for 7 days in head-down position (angle of -8°). The subjects were usually awake in the daytime; they listened to the radio, music; they read, conversed and (if they so desired) slept. Their diet was high in proteins.

We measured body temperature under the tongue using a medical mercury thermometer (0.1°C graduations on the scale). We took their temperature during the waking period, from 0700 to 2300 hours, at 2-h intervals (i.e., at odd

hours) and once during the sleep period (at 0300 hours), for which the subjects had to be wakened.

We compared the results obtained at the main stage to the background values. At the background stage, the parameters were recorded for the 3 days preceding the study. At that time, the subjects were less restricted in motor activity; they usually read sitting in a chair; occasionally they took leisurely walks, spent time in bed. In other respects both stages were identical.

Upon analyzing the data obtained at both stages, we were impressed, first of all, by body temperature in the acrophases of its circadian cycle. We made a note of the maximums daily on the temperature curve, then calculated the arithmetic means of daily maximums for both stages. Similarly, we determined the arithmetic means of daily minimums. We then analyzed the amplitude of the 24-h curves: for each day we calculated the difference between maximum and minimum body temperature, then the daily amplitude was averaged for each stage, i.e., for the background and main stages of the study. In addition, by averaging the figures at each point on the 24-h scale (corresponding to the temperature chart), we calculated two curves for each subject: mean background 24-h temperature and mean daily temperature referable to the main stage of the study. We plotted both curves for each subject on the same chart, then compared them visually.

Results and Discussion

Tables 1 and 2, and the Figure illustrate the results obtained.

Table 1. Daily maximum and minimum body temperature (°C) of subjects at both stages of the study (for each stage the arithmetic means and mean error are given)

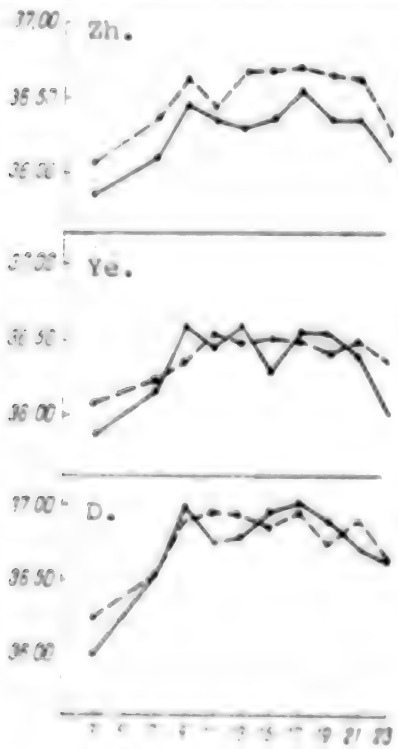
Subject	Background		Antiorthostatic position	
	minimum	maximum	minimum	maximum
D.	36.00±0.03	37.10±0.06	36.23±0.08	37.04±0.04
Ye.	35.86±0.03	36.60±0.06	36.04±0.02	36.66±0.02
Zh.	35.77±0.06	36.80±0.06	36.03±0.03	36.87±0.04

As can be seen in Table 1, the daily temperature minimums were higher in all subjects in antiorthostatic position than at the background stage. The difference in all subjects constituted a mean of 0.22°C, and it was statistically significant ($P<0.05$). Let us mention that the daily temperature minimums were referable in most cases to the nighttime at both stages of the study (0300 hours). As for the daily maximums, which were consistently demonstrable in the daytime, we failed to observe a consistent difference between the period of BR and background stage: the daily

temperature maximums were somewhat lower in one subject (D.) in antiorthostatic position than at the background stage (by a mean of 0.06°C), and in the other two they were slightly higher (by a mean of 0.065°C).

Table 2. Circadian rhythm of body temperature (°C) at different stages of the study (averaged data for each stage)

Time of day (hours)	Subject					
	D.		Ye.		Zh.	
	backgr.	antiorth.	backgr.	antiorth	backgr.	antiorth.
3.00	36.00	36.23	35.86	36.09	35.86	36.[illegible]
7.00	36.53	36.54	36.16	36.23	36.10	36.3[illegible]
9.00	37.00	36.90	36.60	36.39	36.46	36.63
11.00	36.76	36.96	35.46	36.55	36.36	36.44
13.00	36.[illegible]	36.94	36.60	36.49	36.30	36.68
15.00	36.96	36.87	36.30	36.52	36.36	36.[illegible]
17.00	37.03	36.97	36.57	36.50	36.56	36.[illegible]
19.00	36.90	36.73	36.56	36.42	36.36	36.66
21.00	36.73	36.81	36.40	36.50	36.36	36.63
23.00	36.63	36.62	36.03	36.38	36.10	36.29



Dynamics of body temperature at different stages of study. Solid line, averaged parameters of background stage; dash line, averaged parameters in antiorthostatic position.
X-axis, Ulan-Bator time (hours);
y-axis, body temperature (°C)

Thus, the daily temperature minimums were more sensitive to antiorthostatic position than the daily maximums. Since the former coincided more often with the nighttime and the latter occurred only in the daytime, we cannot rule out the possibility that this pattern is a special manifestation of the general biorhythmological law, according to which the reaction of man (as well as animals) to any factor is not the same in the daytime and nighttime. In this case, it may be assumed that man's sensitivity (according to his temperature reaction) to antiorthostatic position is greater at night than during the day. However, this hypothesis requires verification.

In antiorthostatic position, the amplitude of daily temperatures decreases in all subjects (by a mean of 0.20°C); it constituted a mean of 0.10, 0.74 and 1.03°C in subjects D., Ye. and Zh., respectively, in the background period and 0.81, 0.62 and 0.84°C

in antiorthostatic position. It must be noted that the amplitude decreased the most on the 1st-3d days of BR. In view of the reported results, it should be considered that the decrease in amplitude was attributable to elevation of daily temperature minimums.

As can be see in Table 2 and the figure, in addition to the changes mentioned in antiorthostatic position, we observed elevation of body temperature in the course of the day in subject Zh. due to elevation of both nighttime and daytime levels. The curves for the main stage of the study for subjects Ye. and D. were visibly flattened, as compared to the background ones. The cause of this flattening was elevation of nocturnal at 0300 hours) levels, whereas the daytime temperatures fluctuated over virtually the same range on the averaged curves for the background and main stages (see Figure) in each of these two subjects. If we were to calculate the arithmetic means of temperatures of subjects Ye. and D. at both stages of the study, using the data in Table 2, in the interval between 0900 to 2100 hours, no difference would be found between the background (36.50 and 36.88) and main (36.48-36.88) stages.

Thus, in our studies there were changes in some of the initial characteristics of circadian rhythm of body temperature that were associated with spending 7 days in antiorthostatic position (-8° angle of inclination): increase in numerical values of minimums, decrease in amplitude and, additionally in one subject elevation of temperature during the day. If we consider that head-down position at an angle of -8° reproduces, at least in part, the effect of redistribution of blood in weightlessness, one would think that such redistribution during a space flight must be associated with analogous changes in circadian rhythm of body temperature.

The fact that a head-down position at an angle of -8° leads to impairment of circadian rhythm of body temperature enables us to classify this factor as a stressor and, since "desynchronosis" is a mandatory component of the stress syndrome [1], there is every reason to consider antiorthostatic position as a desynchronizer of vital rhythms.

The phenomenon of distinct elevation of body temperature at the points of the daily minimum or (which is the same thing) at night, which we observed in antiorthostatic position, is of the greatest interest. This phenomenon confirms, once more, the thesis that is well-known in biorhythmology, according to which one can gain the fullest information about body reactions to stress agents by examining these reactions at different times of day, including the night. This is an exceptionally fruitful route, in both clinical and research practice.

BIBLIOGRAPHY

1. Alyakrinskiy, B. S. "Fundamentals of Scientific Organization of Work and Rest for Cosmonauts," Moscow, 1975.

2. Alyakrinskiy, B. S. in "Problemy vremennoy organizatsii zhivykh sistem" [Problems of Time Organization of Living Systems], Moscow, 1979, pp 8-36.

3. Makarov, V. I. Ibid, pp 70-74.

4. Stepanova, S. I. "Pressing Problems of Space Biorhythmology," Moscow, 1977.

5. Afanas'yev, A. L.; Bel'tyukov, V. I.; and Kolychev, V. P. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 117-119.

6. Geykhman, K. L.; Gusev, A. N.; Degtyarev, P. G.; et al. Ibid, pp 127-130.

7. Geykhman, K. L., and Mogendovich, M. R. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1977, pp 74-75.

8. Kovalenko, Ye. A. Ibid, No 4, pp 3-8.

9. Mikhaylov, V. M.; Alekseyeva, V. P.; Kuz'min, M. P.; et al. Ibid, No 1, 1979, pp 23-28.

HISTOSTRUCTURAL CORRELATIONS IN THE HYPOTHALAMUS-HYPOPHYSIS-KIDNEYS SYSTEM UNDER HYPOKINETIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 62-67

[Article by I. P. Chernov, V. A. Babayeva and A. G. Gaffarov, submitted 30 Nov 78]

[English abstract from source]

The type and level of morphological changes in different components of the hypothalamic-pituitary-renal system were studied in male rats exposed to 3-month hypokinesia. A correlation between fragmentation of the intercalations and convolutions of renal collecting tubules and histophysiological parameters of the antidiuretic hormone production and secretion was established. Morphological manifestations of increased water permeability of collecting tubules recorded on test days 1—10 and 30—60 were seen together with enhanced activity of the hypothalamic supraoptic nucleus. Possible mechanisms involved in changes of the renal water excretory function during hypokinesia are discussed.

[Text] Restriction of motor activity of man and animals elicits an increase in diuresis leading to dehydration of tissues and the body [1]. Diminished efficiency of antidiuretic mechanism of regulation of fluid-excreting renal function is mentioned among the most important causes of "hypokinetic" polyuria [2, 3]. It is assumed that the effect described as renal "evasion" of the influence of antidiuretic hormone (ADH) is particularly manifest at the early stages of hypokinesia [4]. A. G. Ginetsinskiy [5] established that acid mucopolysaccharides of the interstitium, intercellular cement of terminal parts of the nephron and collecting tubules are the substrate of ADH action. The latter, by means of hyaluronidase, induces depolarization of acid mucopolysaccharides, which renders the walls of the collecting tubules pervious to fluid. Histochemically, this is associated with decrease in or disappearance of acid mucopolysaccharides. This hypothesis was experimentally substantiated in numerous studies conducted in subsequent years [6-8]. The presence of a correlation between morphological changes in the kidneys and level of ADH secretion makes it possible to determine whether indeed there is "evasion" of hormonal influence of the hypothalamus by the kidneys under hypokinetic conditions.

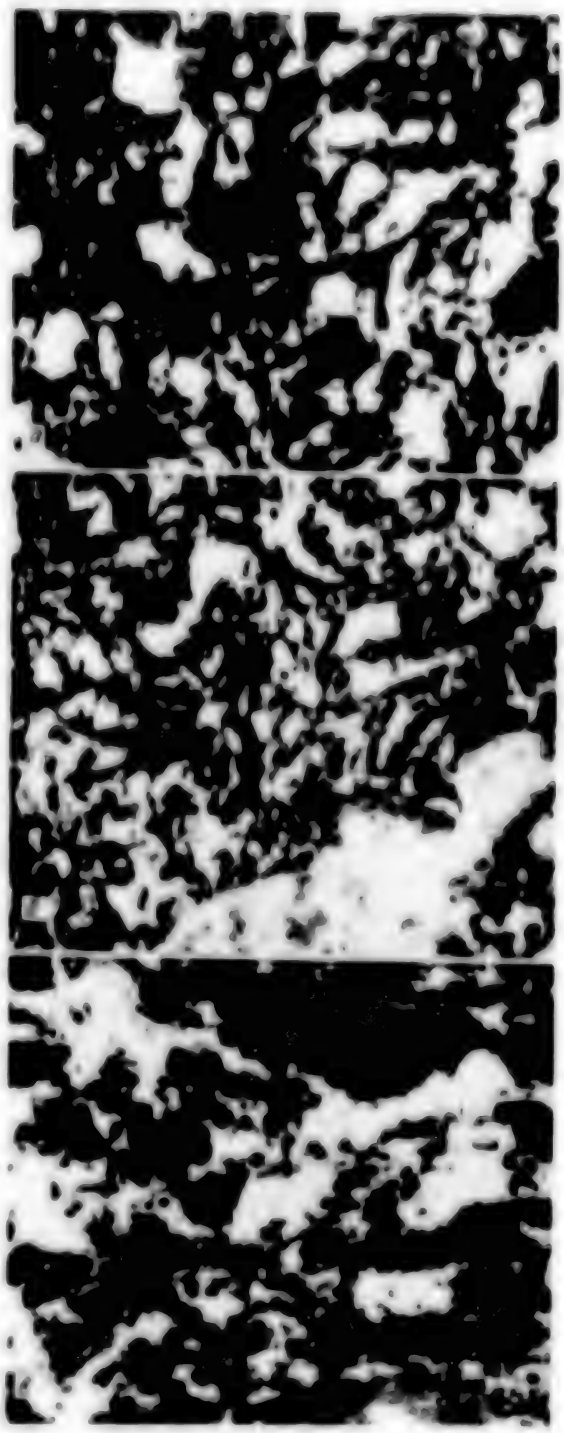
Our objective here was to determine the direction and extent of coordination of morphological changes in different elements of the hypothalamohypophyseorenal system in the course of 3 months of hypokinesia. We examined the supraoptical nucleus (SON) of the hypothalamus and posterior lobe of the hypophysis, which are responsible for production and secretion of ADH [9], as well as the interstitium of the medullary zone and collecting tubules of the kidney, which are the area of application of this hormone [5].

Methods

The experiment was conducted on 90 male mongrel albino rats with an initial weight of 150-170 g. To create hypokinetic conditions, the animals were put in box-cages that restricted movement in all directions. The rats were decapitated after 3 h, then on the 1st, 3d, 5th, 10th, 20th, 30th, 45th, 60th, 75th and 90th experimental days. The hypothalamic region of the brain and hypophysis were fixed in Bouin's fluid and the kidney in Carnoy fluid with 10% neutral formalin. Frontal sections of the hypothalamus and sagittal sections of the hypophysis were stained with aldehyde-fuchsin according to Gomori in the modification of V. F. Mayorova [10] for demonstration of neurosecretions. Nucleic acids were demonstrated with chrome-alum gallocyanin [11]. Secretory activity of SON neurons was determined according to Gomori-positive granule content of neurosecretions [9] and size of nuclei thereof [12, 13]. We calculated the percentage of cells in a state of "rest and start of synthesis" (type I), cells in a "filling" state (type II) and in an "emptying" or "high activity" state (type III) in 8 fields of vision in preparations from each of 5 animals. The type IV cells were "pyknomorphic" or degenerative. An MOV-1-15x screw-type ocular micrometer was used for morphometry of SON neuronal nuclei. We measured the large (L) and small (B) diameters of the nuclei; volume was determined by the formula: $V = \pi/6\ LB^2$. At each observation time we measured 100 nuclei from each of 5 rats. The results of counts and measurements were processed by the method of variational statistics [14], and reliability was determined according to Student (with $P<0.05$). Frozen sections were stained by the Hale method using dialyzed iron; paraffin sections were stained with phosphate-citrate buffer solution of toluidine blue at pH of 4.0, 3.8, 3.6, 3.4, 3.2 and 3.0. Concurrent treatment of sections with hyaluronidase served as a control of the reaction. At different stages of hypokinesia, determination was made of the volume of epithelial nuclei of collecting tubules using the above-described technique.

Results and Discussion

For the first 10 days of the experiment we observed dilatation of the capillary network, swelling of neurons and intensification of their reaction for RNA. At the same time, there was a change in percentile ratio between cells according to distribution and levels of Gomori-positive neurosecretory granules contained in them (Table 1). Starting at the first observation time there was a statistically significant decrease in percentage of type I cells and increase in number of type III cells, which



showed increased production of neurosecretory substance and elimination from perikaryons [9]. Concurrently, there was an increase in mean volume of neuronal nuclei. In intact rats it constituted 199.1± 1.020 μm^3, and increase to 242.1±1.023 μm^3 ($P<0.001$) after 3 h of hypokinesia. The maximum increase in mean volume of nuclei was recorded on the 3d day of hypokinesia (271.6± 1.026 μm^3). The mean volume of nuclei gradually decreased on the 5th and 10th experimental days, but was still reliably greater than the base level (230.1±1.279 and 209.4± 1.018 μm^3, respectively). By the 20th day of the experiment the correlation between all types of cells in SON and mean volume of their nuclei did not differ from control data.

On the 30th-60th days of hypokinesia there was a second wave of increase in functional activity of neurosecretory cells of the hypothalamic SON, as a result of which there was another increase in percentage of cells in the "emptying" or "high activity" stage. During this period there was a decrease in number of cells not only of type I, but type II, which was indicative of relative prevalence of secretion over synthesis. There was more moderate swelling of nuclei at this time. On the 30th

Figure 1.
Neurosecretion content of posterior lobe of hypophysis in intact rat (*a*), on 3d (*б*) and 90th (*в*) days of hypokinesia. Aldehyde-fuchsin stain; objective 40×, ocular 15×.

Table 1. Percentage of different types of neurons in rat hypothalamic SON under hypokinetic conditions (M±m)

Observation time	Types of neurons			
	I	II	III	IV
Control	62.3±1.6	12.0±0.6	13.4±0.4	12.3±0.8
3 h	45.0±1.4 $P<0.001$	8.4±1.0 $P<0.02$	31.3±1.4 $P<0.001$	15.3±0.6 $P<0.02$
3d day	21.8±1.3 $P<0.001$	21.7±1.6 $P<0.001$	37.1±1.6 $P<0.001$	19.4±1.7 $P<0.02$
10th "	40.0±0.4 $P<0.001$	13.2±1.1 $P>0.2$	33.6±0.8 $P<0.001$	13.2±2.2 $P>0.5$
20th "	58.5±0.6 $P>0.2$	12.7±2.3 $P>0.5$	31.7±2.0 $P>0.5$	17.1±2.7 $P>0.1$
30th "	45.7±0.7 $P<0.001$	7.9±0.4 $P<0.001$	38.2±0.5 $P<0.001$	31.1±0.5 $P<0.001$
Control	58.1±2.1	9.9±1.3	16.6±2.2	15.4±1.2
60th day	46.3±1.4 $P<0.001$	2.7±0.4 $P<0.001$	36.3±1.2 $P<0.001$	14.7±0.5 $P>0.5$
75th day	59.4±1.4 $P>0.5$	4.0±0.4 $P<0.01$	17.8±1.3 $P>0.5$	18.8±0.7 $P<0.05$
Control	59.4±3.3	9.9±0.9	15.8±3.1	15.9±1.1
90th day	54.1±1.7 $P>0.1$	17.0±0.2 $P<0.001$	2.8±1.2 $P<0.001$	26.1±1.6 $P<0.001$

Note: P refers to significance of difference between experimental and control rats in percentage of SON cells

day, the mean nuclear volume was 208±1.019 μm^3; it was 224±1.024 μm^3 on the 45th day and 218.8±1.035 μm^3 on the 60th day. At this time, the volume of nuclei in control rats constituted 201.6±1.031 μm^3. At the final stage of the experiment (75th and 90th days of hypokinesia), there was a gradual decrease in actively functioning SON neurons, increase in number of retracted hyperchromic and degenerative cells, associated with decrease in mean volume of nuclei (to 194.6±1.026 μm^3 on the 75th day and 150±1.027 μm^3 on the 90th day, versus 207.6±1.028 μm^3 in the control). At these times, granules of Gomori-positive substance and accumulations thereof were demonstrable along the course of the hypothalamohypophyseal tract. On the first 5 days of restricted movement, the posterior lobe of the hypophysis showed a decrease in overall amount of neurosecretory material, decrease in number and size of Herring's collecting bodies (Figure 1). These changes occurred against the background of dilatation of capillaries, swelling of pituicytes and their nuclei. Thereafter, there was gradual saturation of collecting bodies

with neurosecretory granules, increase in number of granular terminals in the hypothalamohypophyseal tract. During the period of the second increase in hypothalamic SON activity (30th-60th days), there was less marked decrease in neurosecretory substance of the posterior lobe of the hypophysis than at the early stage of restricted movement.

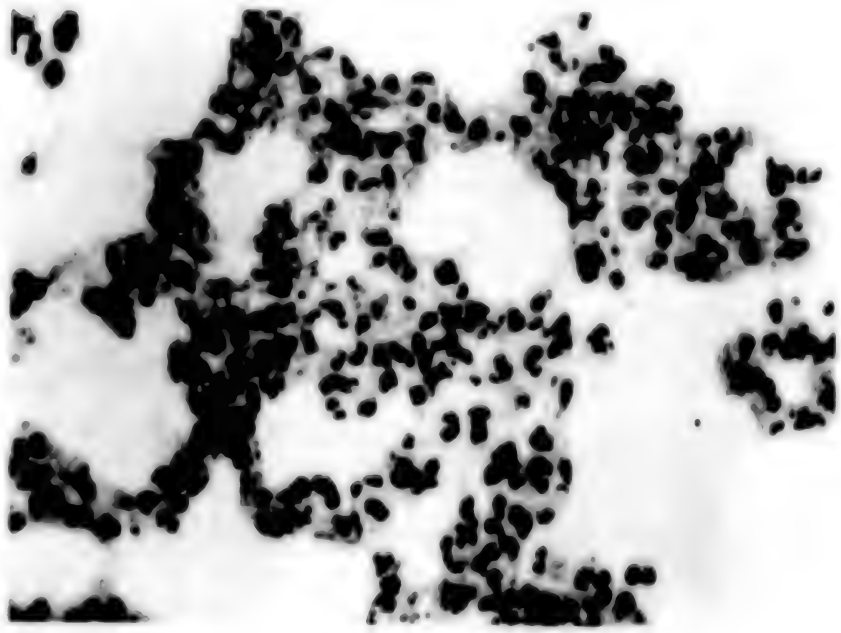


Figure 2. Flattening of epithelium and appearance of apocrinia thereof in collecting tubules of rat kidney on 3d day of hypokinesia; staining according to Selye; objective 40×; ocular 15×

Thus, according to the results of histophysiological analysis, hypokinesia causes phasic changes in neurosecretion of hypothalamic SON. The periods of increased functional activity in the course of the experiment alternated with periods of normalization and decrease thereof. Examination of the kidney revealed that the polysaccharide system of its glomerules and medullary interstitium were highly sensitive to hypokinesia. We demonstrated γ-metachromasia at the sites of localization of Hale-positive substances, which is indicative of the presence of hyaluronic acid. At the early stages of hypokinesia (3 h, 1st and 3d days), there was a decrease in Hale-positive substances, both in the glomerules and interstitial tissue of the

medullary layer of the kidney. The reaction was mildest around the collecting tubules of the internal medullary zone. Staining with toluidine blue revealed a decrease in intensity of γ-metachromasia also in the areas with low content of Hale-positive substances. On the 5th experimental day, the amount and distribution of acid mucopolysaccharides in the kidney of experimental rats were close to control levels. By the 10th day of hypokinesia, there was a second and more marked decrease in intensity of staining, and attenuation thereof was observed in both the internal and external medullary zones. Thereafter, normalization of the reaction (on the 20th day) was again followed by a period of decreased intensity of staining (30th, 45th and 60th days). This decline was less marked than at the early stage of hypokinesia. By the 90th day of restricted mobility, there was a significant increase in number of structures showing an intensive reaction for acid mucopolysaccharides in the medullary layer of the kidney.

In the course of hypokinesia for 3 months, there were also changes in the epithelium of the collecting tubules. Thus, on the 1st-10th experimental days, when there was attenuation of the reaction for acid mucopolysaccharides, there was an increase in number of collecting tubules with flattened epithelium; we observed sloughing off of the apical ends of the cells and protrusion of nuclei into the tubular lumen (Figure 2). These changes in the epithelium, like the mild reaction for acid mucopolysaccharides, are the morphological equivalent of antidiuresis [5, 15]. The volume of epithelial nuclei is a reliable criterion for evaluation of the functional load on the nephron [16]. The results of karyometry of the epithelium of collecting tubules are listed in Table 2. They graphically demonstrate that the increase in mean volume of nuclei occurs at the times when one observes morphological signs of activation of facultative reabsorption of fluid.

Table 2. Volume of epithelial nuclei in collecting tubules under hypokinetic conditions (M±m)

Day of observation	Experiment	Control	P
1	71.12±1.020	67.76±1.026	<0.05
3	73.26±1.019	» »	<0.01
5	69.50±1.021	» »	>0.2
10	75.34±1.017	» »	<0.001
20	70.04±1.014	» »	>0.1
30	75.51±1.030	69.07±1.017	<0.01
60	66.63±1.033	72.18±1.026	<0.001
90	72.78±1.028	73.62±1.021	>0.5

Note: P indicates significance of differences between experiment and control with regard to volume of nuclei.

A comparison of the results of examining the kidney to findings of histophysiological studies of activity of SON of the hypothalamus and neurohypophysis shows that morphological signs of permeability to water were observed in the collecting tubules against the background of increased activity of the hypothalamohypophyseal neurosecretory system. Consequently, ADH exerts its inherent influence in the presence of hypokinesia as well. However, in spite of the increased ADH secretion and efficiency of its influence on permeability of collecting tubules, increased diuresis was still observed under hypokinetic conditions. What is the cause of this phenomenon? First of all, intensification of glomerular filtration [2, 17], which was demonstrated under these conditions, is important. Moreover, facultative reabsorption of fluid occurs with normal function of all elements of the counterflow system, which requires an optimum rate of movement of fluid over the tubules and straight vessels of the medullary layer of the kidney [18]. In this case, there is accumulation in the medullary layer of osmotically active substances and increase in corticomedullary gradient. The faster renal blood flow, which occurs when movements are restricted [17, 19], results in having sodium, chlorine, urea flushed from vessels (and, consequently, from tissue), as well as drastic decrease in renal capacity to absorb fluid [18].

In conclusion, it should be noted that a number of systems that participate in fluid-excreting function of the kidney are directly or indirectly involved in changing this process under hypokinetic conditions. Thus, the renin-angiotension system, activation of which has been observed under hypokinetic conditions [20], is important to the mechanism of accelerating renal blood flow. Evidently, hypercalcemia, which is also present under these conditions [21], is also implicated. It has been shown [22] that hypercalcemia diminishes reabsorption of osmotically free water as a result of redistribution of intrarenal blood flow, vasodilation of rectus vessels of the medullary substance, decreased transport of urea from the collecting tubules and salts in Henle's loop.

BIBLIOGRAPHY

1. Kovalenko, Ye. A. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1976, pp 3-14..
2. Pak, Z. P., et al. Ibid, No 4, 1973, pp 56-59.
3. Grigor'yev, A. I., et al. Ibid, No 4, 1976, pp 55-59.
4. Andrianova, L. A. Ibid, No 5, 1971, pp 26-29.
5. Ginetsinskiy, A. G. "Physiological Mechanisms of Fluid-Electrolyte Equilibrium," Moscow--Leningrad, 1963.
6. Mashanskiy, V. F., et al. TSITOLOGIYA [Cytology], No 1, 1966, pp 23-29.

7. Natochin, Yu. V. PROBL. ENDOKRINOL. [Problems of Endocrinology], No 4, 1968, pp 118-126.

8. Ivanova, L. N. "Analysis of the Mechanism of Action of Antidiuretic Hormone on the Mammalian Kidney," doctoral dissertation, Novosibirsk, 1972.

9. Polenov, A. L. "Hypothalamic Neurosecretion," Leningrad, 1968.

10. Mayorova, V. F. ARKH. ANAT. [Archives of Anatomy], No 8, 1960, pp 101-103.

11. Pearse, A. G. E. "Histochemistry," Moscow, 1962.

12. Voytkevich, A. A. "Neurosecretion," Leningrad, 1967.

13. Aleshin, B. V.; Demidenko, N. S.; and Mamina, V. V. ARKH. ANAT., No 10, 1974, pp 29-33.

14. Khesin, Ya. Ye. "Size of Nuclei and Functional State of Cells," Moscow, 1967.

15. Vinnichenko, L. N., et al. ARKH. ANAT., No 8, 1973, pp 61-68.

16. Zufarov, K. A.; Gontmakher, V. M.; and Khidoyatov, B. A. "Cytofunctional Distinctions of the Kidney," Tashkent, 1974.

17. Grigor'yev, A. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 6, 1972, pp 828-835.

18. Natochin, Yu. V. "Ion-Regulating Function of the Kidney," Leningrad, 1976.

19. Kozyrevskaya, G. I. "Effect of Experimental Restriction of Muscular Activity and Space Flight Factors on Fluid-Electrolyte Metabolism in Man," author abstract of candidatorial dissertation, Moscow, 1970.

20. Polyak, M. G., et al. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 139-141.

21. Biryukov, Ye. N. "Change in Mineralization of Bone and Calcium Balance Under Experimental Hypokinetic Conditions and in Space Flights," candidatorial dissertation, Moscow, 1968.

22. Kulayev, D. V. "Mechanism of Parathyroid Polyuria," author abstract of candidatorial dissertation, Ordzhonikidze, 1969.

UDC: 612.273.2.017.2:612.223.1.017.1

EFFECT OF CONDITIONING ANIMALS FOR HYPOXIA ON THEIR RESISTANCE TO POISON INHALATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian, No 4, 1980 pp 67-71

[Article by G. P. Tikhonova and G. I. Solomin, submitted 12 Jun 79]

[English abstract from source]

The rats trained to hypoxic hypoxia changed their resistance to the inhalation effect of dioxane and dichloroethane vapors. The training regimes (20-day continuous hypoxia at an altitude of 3,200 m and intermittent hypoxia for 6 hours a day amounting to 25 rises to an altitude of 5,000 m) influenced markedly the intoxication effect. Adaptation to hypoxia increased the alveolar-capillary surface of the lung parenchyma thus enhancing a better entry of chemicals into the body. The posthypoxic pattern of the structural rearrangement of the pulmonary tissue was similar to that observed during moderate hyperoxia.

[Text] It has been experimentally shown that an organism conditioned for hypoxic hypoxia can have greater resistance to a number of deleterious environmental factors. However, there are still many unclear and contradictory elements concerning resistance to the effect of toxic agents that are inhaled [1-3]. This is a timely question, since hypoxia is used in training humans for specific activities in pressurized compartments where there may be accumulation of high concentrations of chemical compounds in the air environment in case of accident.

We submit here the results of a study of the resistance of albino rats to chronic inhalation of dioxane and dichloroethane (DCE) after continuous and intermittent adaptation to hypoxic hypoxia. The choice of agents was governed by the fact that they could possibly be contained in the artificial atmosphere of airtight compartments, in the construction of which polymer materials are used [4].

We made a comparative analysis of the morphological structure of lung tissue and its vascular system immediately after exposure to hypoxia in different modes and at different stages of the aftereffect period in order to substantiate the causes of changes in animal resistance to poisoning due to inhalation of chemical compounds.

Methods

The rats were conditioned to hypoxia in a pressure chamber using two modes: 20-day, around the clock in the pressure chamber at an "altitude" of 3200 m (the animals were "brought down" for 1 h every 48 h to clean their cages and fill feeders) intermittent exposure to an "altitude" of 5000 m for 6 h/day for 5 days a week (a total of 25 "climbs"). The ascent was performed in 3 days, starting at an "altitude" of 2000 m.

We tested the animals' resistance to chemicals on the day they were removed from the pressure chamber, as well as on the 1st, 7th, 15th and 21s days of the aftereffect period. We used 800-liter chambers to deliver inhalations for 4-h at a time, using dioxane in concentrations of 34±0.7 mg/ℓ and DCE in concentrations of 6.7±0.06 mg/ℓ. A quantitative assay of the chemicals in the chambers was made by the method of gas chromatography (A. I. Gorshunova conducted the analysis); in some cases we used an estimation method. By the end of the inhalation period, oxygen content constituted 19-20% and humidity ranged from 65 to 85%.

Pathomorphological studies were made using conventional methods for histological staining of the lungs, and we submitted alveolar tissue to morphometry. We filled the vascular system of the lungs with a solution of India ink and gelatin.

Results and Discussion

Analysis of the data pertaining to rat resistance to high concentrations of chemicals revealed that animal mortality was 20-30% higher after inhalation of dioxane in both modes of hypoxia than in the control. The results with DCE depended on conditioning mode: continuous adaptation diminished rat resistance (6 out of 10 animals submitted to hypoxia died on the 2d postinhalation day, versus 2 in the control), whereas intermittent conditioning increased their resistance to poisoning (all of the experimental animals survived, whereas 8 out of 10 control rats died).

As we know, the toxic effect of agents depends to a significant extent on the condition of target systems of the organism. In the case of inhalation thereof, we thought it was important to obtain a microstructural description of lung tissue following different modes of conditioning the animals to hypoxia.

A comparative examination of the lungs revealed that prolonged conditioning of the rats led to a substantial change in their structural organization, and the morphology of this organ presented distinctions related to the different conditioning modes. A distinct reaction referable to the vascular system of the lungs was prominent in all rats. There was an increase in length of the vasocapillary network due to tortuosity of vessels, elongation of venous segments, appearance of additional arteriovenous anastomoses and vascular loops, increase in number and diameter of

functional capillaries. Hypertrophic changes in the walls of vessels of all calibers were inherent in all animals. However, while daily "ascents" led to muscularization of arterial and venous walls and increase in their elastic elements, after uninterrupted exposure to hypoxia we found mainly thickening of the adventitia due to splitting [of fibers] and swelling. The latter was particularly marked in blood vessels of medium caliber, and it was indicative of impairment of their permeability. It should be noted that macrophages disappeared almost entirely from the adventitia after continuous hypoxia, unlike intermittent exposure. There was drastic reduction of lymphoid elements in the peribronchial lymph node. This fact perhaps renders an organism conditioned to hypoxia more susceptible to inflammatory and infectious lung diseases, which has been repeatedly mentioned in the literature [5]. The media of the vascular wall of arterioles and venules in the rat lung also presented swollen connective tissue fibers and membranes after continuous exposure to high "altitude." In a number of cases, the muscle bundles in veins were thinned down. Such changes in vascular walls could render them more fragile and vulnerable.

Constriction of arteriolar lumen, as well as spastic capillaries, were observed in the first hours after exposure to hypoxia. This was demonstrated both with the usual methods of staining tissues and injection of the vascular bed with India ink. However, most animals already presented uneven dilatation and plethora of the capillary system of the lung on the 2d day.

Conditioning to hypoxic conditions led to an enlargement of the internal surface of bronchi and bronchioles, as well as reduction in number of nonfunctional "spare" alveoli. Areas of functional emphysema appeared. Morphometric findings showed that there was greater increase in mean large diameter of alveoli of rats after intermittent adaptation to hypoxia than after continuous exposure: $D = 0.13 \pm 0.02$ mm with intermittent hypoxia, $D = 0.11 \pm 0.04$ mm with continuous exposure and $D = 0.09 \pm 0.02$ mm in control animals.

Thus, histological and morphometric studies of lung tissue after different modes of adaptation to hypoxia revealed enlargement of overall surface of functional vessels and capillaries, as well as ventilated area of alveolar surface, which should help increase diffusion capacity of the lungs. Some features of the structural changes we found in the lungs were also noted in the works of other authors [6, 7]. These changes are among the body's adaptive reactions to hypoxia. At the same time, enlargement of the surface of alveoli and capillaries could be instrumental in greater access of toxic substances. It should be expected that intensification of intoxication would be manifested primarily with regard to agents with cumulative properties. Of the compounds we tested, dioxane has such properties: it is rapidly absorbed, and remains in the organism for a long time. Evidently, this is one of the causes of diminished resistance to it in all conditioned rats. DCE is eliminated quite rapidly, and up to 40% of the taken dose is eliminated through the lungs. It can be assumed that the increase

in diffusion capacity of the lungs should not have an appreciable effect on degree of DCE poisoning. However, the experimental results revealed that there was a change in animal resistance to DCE: after continuous conditioning the rats' resistance diminished and, conversely, after intermittent exposure it increased. Postmortem examination of rats that died after inhalation of the toxic agent revealed that the chief causes of death were hemorrhages and edema of the lungs. Perhaps, the dissimilar structural organization of vascular walls following different modes of conditioning to hypoxia was instrumental, to some degree, in causing differences in rat resistance to DCE. It should be borne in mind that, following adaptation to hypoxia, resistance determines not only the morphofunctional state of the respiratory system, but resistance of other organs to intoxication. As for the tested agents, it is known that both DCE and dioxane are narcotic compounds. Moreover, DCE impairs liver function, while dioxane is toxic to the kidneys [8].

Pathomorphological examination of the lungs in the posthypoxia period revealed that after the animals were returned to the usual atmospheric conditions the structural organization of the parenchyma of this organ continued to undergo changes for a long time, and there were some differences related to conditioning modes. On the 2d day, all rats presented hypersecretion of mucus in the bronchi, collapse of some alveoli and appearance of atelectases with hyperemia of capillaries in them. There was focal perivascular edema. All these signs were more marked in the rats exposed to hypoxia around the clock. On the 7th day of the aftereffect period, we observed irregular plethora of the venous-capillary network with spasm of small arteries; occasionally there was diapedetic migration of erythrocytes. There was an appreciable decrease in mean large alveolar diameter (0.095 ± 0.04) in rats submitted to continuous hypoxia, which was attributable to collapse of their walls over considerable segments of the lobes. An increase in tortuosity and dissolution of elastic fibers in alveolar septa were demonstrated by a special staining technique (Weigert's). After intermittent conditioning, there was focal atelectasis of tissue at the base of the lobes, where blood flow and ventilation were higher, whereas in the apical segments there was persistence of emphysematous dilated alveoli with constricted capillaries. The mean large diameter of the alveoli remained increased (0.12 ± 0.03).

The nature of the changes demonstrated in pulmonary parenchyma on the 2d and 7th days after exposure to hypoxia was similar to the morphological reaction that is usually observed with moderate hyperoxia [9, 10]. It can be assumed that, in rats that are functionally and structurally adapted to an atmosphere with low oxygen content (especially in the case of intermittent exposure), readaptation to the usual conditions proceeds on the order of oxygen poisoning, but of course this requires corroboration with physiological data.

By the end of the 2d-3d week of the posthypoxic period, focal dystrophic and necrotic changes moved to the foreground, both in the respiratory and

vascular system: obliteration of the cavity of some bronchioles and alveoli with atrophy of capillaries in these areas; thinning of muscle fibers in the walls of large and medium-sized vessels, dystrophic changes in elastic tissue. Rats kept in the pressure chamber continuously presented a small-focus interstitial process in perivascular parenchyma, while one of them revealed small inflammatory foci. In the case of intermittent conditioning, there was focal dilatation of air-delivering respiratory bronchioles and alveolar pathways with shortening of alveolar sacs, leading to reduction of area of gas exchange in the acini.

The study of animal resistance at different stages of the posthypoxia period revealed that, while rats submitted to intermittent conditioning did not differ from control animals with regard to resistance to dioxane and DCE by the end of the 3d week, in the case of continuous conditioning the death rate was higher than in the control.

Thus, this study indicates that after conditioning to hypoxic hypoxia there is a change in resistance to toxic agents delivered via inhalation, and the conditioning mode determines, to a significant extent, the effect of such inhalations.

Enlargement of the alveolocapillary surface of pulmonary parenchyma in the course of adaptation to hypoxia causes intake of more chemicals via inhalation.

The nature of structural change in pulmonary tissue and its vascular system in the posthypoxic period is about the same as with moderate hyperoxia.

BIBLIOGRAPHY

1. Belay, V. Ye.; Bryuzgina, M. I.; and Vasil'yev, P. V. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 8, 1968, pp 230-235.

2. Vasil'yev, G. A.; Tiunov, L. A.; and Kustov, V. V. Ibid, Vol 16, 1971, pp 178-182.

3. Tikhonova, G. P.; Solomin, G. I.; Bizin, Yu. P.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1975, pp 27-31.

4. Uands, R. K. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 1, 1975, pp 74-104.

5. Krupina, T. N.; Korotayev, M. M.; Pukhova, Ya. I.; et al. KOSMICHESKAYA BIOL., No 1, 1977, pp 38-42.

6. Rakhimov, Ya. A.; Etingen, L. Ye.; Belkin, V. Sh.; et al. "Morphology of Viscera Under High-Altitude Conditions," Dushanbe, 1968, pp 54-69.

7. Birkun, A. A., and Nemirovskaya, I. N. ARKH. PAT. [Archives of Pathology], No 4, 1975, pp 37-43.

8. Lazarev, N. V., and Levina, E. N. (editors) "Toxic Agents in Industry," Leningrad, 7th ed., Vol 1, 2, 1976.

9. Kaplan, T. P. in "Annual Conference on Atmosphere Contamination in Confined Space," 2d, Ohio, 1966, pp 200-220.

10. Gramenitskiy, P. M. "Conditions and Mechanism of Development of Decompression Disorders," doctoral dissertation, Leningrad, 1967.

UDC: 613.31

EXPERIMENTAL STUDIES OF SETTING STANDARD FOR OPTIMUM SALT COMPOSITION OF POTABLE WATER

Moscow KOSMICHESKAYA BIOLOGIYA i AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 71-77

[Article by L. I. El'piner and O. I. Balashov, submitted 21 May 79]

[English abstract from source]

As known, the concentration of salts in potable water determines water intake in a certain degree. Water with marginal concentrations of salts brings about increased water consumption. This causes tension in the renal and extrarenal excretory mechanisms and, as a result, leads to unjustified (from the point of view of expedient behavior) energy expenditures that are not induced by environmental factors. The optimal variant is water with a salt concentration of 500 mg/l and 250 mg/l. Tap water as well as water with a salt concentration of 100 mg/l occupy an intermediate position between desirable and undesirable waters but lie closer to the optimal variant.

[Text] The comfort of living conditions, health status and efficiency of people, both on the ground and in space flights, depend largely on the correct solution of the problem of water supply.

Markedly desalinated distilled water was found to be unsuitable for long-term intake [1, 2]. This made it necessary to elaborate methods for artificial mineralization of water [1, 3-5]. At the present time, a method has been proposed to adjust the mineral composition of demineralized water by means of graded addition of salt solutions producing drinking water of the hydrocarbonate class [6, 7]. The choice of quantitative and qualitative parameters was based on reproducing the salt composition of unadulterated water, the potability of which was determined by its safety, harmlessness and fitness for consumption [8]. But, as we can see from numerous data [2-5, 9, 10], mineralization of drinking water is a feature that determines the specificity of the body's reactions to drinking water.

We tried to apply general principles and criteria for choosing the optimum variant in order to develop conceptions of optimality of salt composition of water [4, 9, 11].

The thesis that, in determinig the tactics of behavior, the organism chooses the optimum solution in a given situation was expounded by N. Rashevskiy in the form of principle of optimum construction. It is based on the fact that organisms with an optimum biological structure through natural selection are also optimal in the sense that they minimize a certain evaluating function that is determined on the basis of the main features of the environment [12]. Yu. G. Atomonov, who developed the teaching of I. P. Pavlov concerning dynamic equilibrium between the environment and organism, expounded the principle of dynamic adequacy, which states that "with a change in complexity and organization of the environment, a biological system constantly strives to reach a new level of conformity with the environment in complexity and organization, with minimization of time, expenditure of substances and energy" [13]. In this thesis we find specification of the evaluating function based on the general principle of function: minimal outlay of substances and energy, which extends to all aspects of cell metabolism [14].

In general, the mathematical expression of an optimum solution amounts to determination of the extreme value of the sought function, i.e., finding its maximum or minimum. This thesis is already quite evident in definitions of the optimum process of functioning of an organism according to the principle of maximum economy of substances and energy [14]. The principles of optimum design of N. Rashevskiy [12], definition of optimum regulation in biosystems [15] and formulation of the mathematical problem of defining optimum control [16] are analogous.

When solving problems dealing with determination of an optimum variant one must do the following: 1) specify the process to which given theses apply; 2) measure it in comparable units; and 3) single out of all the ratings the extreme that is the optimum [15].

In order to solve the formulated problems, we tried to find a characteristic that would, while having some degree of universality, reflect a real situation related to the effect on the organism of drinking water in one hydrochemical class, but with different level of mineralization. As a criterion, we used the level of energy metabolism, which could be assessed on the basis of amount of feed ingested. This parameter is the generalized characteristic of all types of metabolism [17]; it makes it possible to assess conformity of the tested levels in different experimental groups with the principle of minimal expenditure of energy. Fluid-electrolyte metabolism is closely related to energy metabolism. For this reason, we studied the main routes of regulation of the former wherever the significance of energy expenditure is particularly marked, while the methods of objective control make it possible to obtain comparable figures. We also proceeded from the fact that the organism has various regulatory mechanisms, and self-adjustment of metabolism proceeds in the direction that provides the maximum possible energetic conformity ["conjugation"] under given conditions, and thereby the minimal loss of energy [18].

Methods

We conducted a 5-month experiment on male albino rats with an intial weight of 120-140 g, which were kept on the standard diet recommended by the Institute of Nutrition, USSR Academy of Medical Sciences. The caloric value of the feed constituted 4.11 kcal/g dry substance. Upon oxidation thereof in the organism, 0.514 g of fluid was formed according to the estimates of Schuck [19]. When mixing the constituents of feed, we added 38% water. We took these data into consideration in estimating overall fluid metabolism.

The choice of water samples studied for mineralization was governed by the hygienic standards for quality of drinking water, and they met the requirements of GOST 2874-73. We prepared water samples with total mineralization of 50, 100, 250, 500 and 1000 mg/ℓ using a previously developed method [20]. The animals were divided into 7 groups, each of which was given water of a specific composition: the 1st group was given distilled water; the 2d to 6th groups were given water with mineral content of 50, 100, 250, 500 and 1000 mg/ℓ, respectively; the 7th group was given Moscow tap water. After 3-4 days, the water was replaced with freshly prepared batches, which were decanted into special troughs that prevented contamination and evaporation. As a result of preliminary screening (in addition to the conventional method of forming groups), we eliminated all rats with diuresis differing from normal, as well as animals who demonstrated the feed-hoarding reflex. For 5 months the animals were kept in common gages, in groups, and then in individual metabolic cages, when we recorded daily feed and water intake, daily output of urine and feces after a 2-week period of adaptation to upkeep conditions. During this period, the cages, trays, feeders and urine collectors were washed thoroughly, rinsed in distilled water and dried. The experiment was conducted in a room with ambient mean temperature of +18°C. We assayed urine potassium and sodium on a flame photometer, chlorine according to Shel's [21], and evaluated glomerular filtration in the kidneys according to elimination of endogenous creatinine [22].

Perspiration was assayed as the difference between total fluid intake (drinking water, fluid contained in feed, fluid formed upon oxidation of proteins, fats and carbohydrates of feed in the body) and diuresis indicator. Since determination of perspiration on the basis of 24-h fluid balance is indirect, we made a direct study thereof on another batch of animals maintained under identical conditions. We put 1 rat from each group in perforated plastic cages with urine collectors, and the animals were weighed hourly, together with their cages. The difference in weight between two weighings represented perspiration in 1 h. We made a correction for the amount of urine excreted. We pursued observations of 7 animals (1 from each group) for 8 h per day in order to rule out the influence of daily fluctuations of meteorological factors. From the figure obtained, we determined the daily perspiration.

Among the tested water samples, we included distilled water, the mineral content of which can be considered to be virtually nil. To compare artificial and unadulterated drinking water with similar mineral content, we included Moscow tap water (350 mg/ℓ) in the experiment.

Results and Discussion

The Table lists for each parameter the size of the sample, mean value, standard deviation and Student's criterion in relation to the minimal value for several artificially mineralized waters, which was taken as the optimum variant.

Energy metabolism: In our experiments, feed was the only source of energy. Since there were negligible variations of initial weight, it must be conceded that water with mineral content of 500 mg/ℓ was the optimum variant in the series of water samples tested. There was the lowest energy consumption per 100 g weight. According to this parameter, the groups of animals given water with mineralization of 100 and 250 mg/ℓ was close to the optimum variant.

There was no statistically reliable difference between adjacent animal groups with regard to amount of feed ingested as a function of category of artificially mineralized water. The only exception was the animal group whose water had maximum mineralization. This can apparently be attributed to the fact that the difference in salinity of water was much more marked in the 5th and 6th groups, than between other groups.

The difference in feed intake by animals in groups given water with mineral content of 500 mg/ℓ and distilled water constituted 2.42 kcal. If we consider that water is a factor that is active daily and constantly (i.e., there is summation of the effect as a function of time), the advantage of water with mineralization of 500 mg/ℓ becomes obvious. In assessing the expenditure of energy, it must be noted that it was lowest with intake of water having mineral content of 250 and 500 mg/ℓ (19,8 and 19.7 kcal/100 g weight per day), somewhat higher with intake of Moscow tap water and water with mineral content of 100 mg/ℓ (21.3 and 20.4 kcal/100 g/day), while distilled water and water with mineralization of 1000 mg/ℓ was rated as unsatisfactory (22.1 and 21.5 kcal/100 g/day).

Water intake: Water intake is one of the parameters directly related to energy metabolism. This parameter was highest in groups given demineralized water and water with maximum mineralization. Animals in the group given water with mineral content of 50 mg/ℓ consumed somewhat less water. The animals drank about the same amounts of tap water, as well as water with mineral content of 100 and 250 mg/ℓ. Lowest water intake was noted in the group given water with mineral content of 500 mg/ℓ. A statistically reliable difference was demonstrable only in the group of animals given demineralized water. The difference between other groups was insignificant, and the fact that reliability could not be proven is apparently attributable to the small size of the sample in this case.

In order to determine the true fluid intake, we took into consideration the water contained in feed, as well as endogenous fluid, in addition to drinking water. The Table shows that the group of animals given water with 500 mg/ℓ mineral content drank reliably less of this water than the group of rats given distilled water, or water with mineral content of 50 and 1000 mg/ℓ. With regard to total fluid intake, animals given Moscow tap water, water with mineralization of 100 and 250 mg/ℓ were close to this group. Maximum fluid metabolism was observed in the group of animals given distilled water; as the amount of salts in the water increased there was a decrease in intensity of fluid metabolism in the corresponding groups, and lowest fluid content per unit weight was demonstrated in the group of animals given water with mineral content of 500 mg/ℓ. The level of fluid metabolism in rats given water with 1000 mg/ℓ minerals was close to that of animals that drank water with low mineral content. Increased water intake leads to an increase in expenditure of energy, which is related to subordination of homeostasis, as well as deposition in the organism.

Excretion of fluid and salts in urine: While feed and water intake varied in the same direction, urine output varied differently in the animal groups: with symmetrical distribution of levels, it was slightly shifted in the direction of water with low mineral content. Diuresis was lowest in the group of rats given tap water, it was highest in animals given water with extreme mineral levels.

The distribution of levels of glomerular filtration as a function of the artificially prepared water samples was close to symmetrical, with the center corresponding to water with 250 mg/ℓ minerals. In several of the artificially mineralized water samples, we observed the same patterns as in the preceding cases. There was no significant difference in glomerular filtration between experimental groups of animals that were next to one another with regard to degree of mineralization of drinking water, but the farther away they were from the center of symmetry of this distribution, the more marked the statistical difference according to the criterion of Student. In assessing glomerular filtration as the result of involvement of the kidneys in regulating an optimum endogenous medium, one should consider water with mineral content of 250 and 500 mg/ℓ the best (1.18 and 1.20 mℓ/min, respectively). In the groups of animals given water with mineralization of 0, 50 and 1000 mg/ℓ, this parameter constituted 1.55, 1.39 and 1.61, respectively.

Daily excretion of chlorine and sodium by the kidneys as a function of mineral content of drinking water was similar. The absolute values were in the same order as feed intake. Maximum 24-h excretion of these ions corresponded to the extremes of mineral content of drinking water and the minimum excretion corresponded to moderate mineralization of drinking water (i.e., 250 and 500 mg/ℓ). The group of rats given tap water was close, with regard to absolute value of these parameters, to the group of animals given tap water and water with mineral content of 1000 mg/ℓ.

Parameters of fluid, mineral and energy metabolism in experimental animals given water with different mineralization levels

Parameter	Distilled water	Mineral content of artificially prepared water, mg/l					Tap water
		50	100	150	500	1000	
Animals' weight, g	384,2 ± 15,6 n 10	397,6 ± 22,8 n 10	391,5 ± 19,1 n 10	394,4 ± 16,2 n 10	405,3 ± 25,7 n 9	393,5 ± 26,3 n 8	368,1 ± 19,5 n 10
Daily feed intake, kcal/100 g weight	22,11 ± 0,86 n 80; t 2,60	21,17 ± 0,41 n 80; t 2,86	20,43 ± 0,89 n 80; t 1,20	19,81 ± 0,65 n 78; t 0,22	19,69 ± 0,33 n 69; t 0	21,54 ± 0,41 n 63; t 2,87	21,33 ± 0,51 n 80; t 3,62
Daily water intake, ml/100 g weight	5,54 ± 0,32 n 10; t 3,00	4,32 ± 0,26 n 10; t 1,11	4,06 ± 0,34 n 10; t 0,40	4,04 ± 0,47 n 10; t 0,29	3,88 ± 0,29 n 9; t 0	4,80 ± 0,39 n 8; t 1,87	4,02 ± 0,38 n 10; t 0,39
Daily fluid intake, ml/100 g wt. (drinking water+water in feed+endogenous oxid.water)	11,72 ± 0,18 n 80; t 7,90	10,15 ± 0,17 n 80; t 2,83	9,74 ± 0,35 n 80; t 1,01	9,47 ± 0,16 n 78; t 1,46	9,31 ± 0,21 n 61; t 0	10,64 ± 0,23 n 64; t 3,90	9,85 ± 0,19 n 80; t 1,74
Daily diuresis, ml/100 g wt.	3,25 ± 0,02 n 80; t 3,00	2,96 ± 0,02 n 80; t 0,77	2,83 ± 0,10 n 80; t 0	3,04 ± 0,11 n 79; t 1,00	3,19 ± 0,10 n 78; t 2,10	3,54 ± 0,13 n 64; t 3,58	2,66 ± 0,07 n 79; t 1,67
Glomerular filtration, ml/min	1,56 ± 0,04 n 30; t 6,02	1,39 ± 0,06 n 20; t 3,18	1,28 ± 0,06 n 30; t 1,56	1,18 ± 0,16 n 28; t 0	1,20 ± 0,05 n 26; t 0,36	1,61 ± 0,07 n 24; t 5,65	1,30 ± 0,06 n 25; t 2,79
Daily excr. chlorine in urine, meq/100 g wt.	0,56 ± 0,02 n 29; t 3,63	0,47 ± 0,03 n 29; t 0,92	0,46 ± 0,02 n 28; t 0,90	0,43 ± 0,04 n 29; t 0	0,43 ± 0,03 n 26; t 0	0,57 ± 0,03 n 24; t 3,76	0,54 ± 0,04 n 30; t 2,31
Daily excr. sodium in urine, meq/100 g wt.	0,10 ± 0,0042 n 29; t 2,99	0,09 ± 0,0072 n 29; t 1,13	0,09 ± 0,0041 n 29; t 0,86	0,08 ± 0,0062 n 28; t 0	0,08 ± 0,0054 n 27; t 3,69	0,012 ± 0,0072 n 24; t 3,69	0,10 ± 0,0044 n 30; t 1,95
Daily excr. potassium, meq/100 g wt.	0,13 ± 0,060 n 30; t 4,00	0,12 ± 0,004 n 29; t 2,44	0,10 ± 0,007 n 30; t 0	0,10 ± 0,006 n 29; t 0	0,10 ± 0,006 n 26; t 0	0,13 ± 0,008 n 24; t 3,44	0,15 ± 0,007 n 30; t 5,30
Daily perspiration (indirect), ml/100 g wt.	8,53 ± 0,18 n 80; t 11,51	7,22 ± 0,12 n 78; t 7,05	6,98 ± 0,17 n 80; t 4,60	6,43 ± 0,15 n 78; t 2,20	6,07 ± 0,12 n 60; t 0	7,07 ± 0,19 n 64; t 4,69	7,20 ± 0,13 n 79; t 2,71
Daily perspiration (direct measurement), ml/100 g wt.	5,04 ± 0,19 n 62; t 3,78	4,80 ± 0,17 n 62; t 3,21	4,56 ± 0,14 n 62; t 2,82	4,32 ± 0,17 n 63; t 1,35	4,08 ± 0,12 n 63; t 0	4,56 ± 0,19 n 63; t 2,06	4,32 ± 0,17 n 63; t 0,47
Daily energy expendit. minus energy of perspiration, kcal/100 g	17,16 ± 0,87 n 80; t 1,10	16,99 ± 0,41 n 80; t 1,33	16,38 ± 0,51 n 80; t 0,44	16,08 ± 0,45 n 78; t 0	16,21 ± 0,33 n 69; t 0,21	17,44 ± 0,42 n 63; t 1,44	17,15 ± 0,63 n 80; t 1,09

The direction of changes in excretion of potassium, sodium and chlorine in urine was the same in animals given the series of artificially mineralized water samples as the levels of glomerular filtration, i.e., the mechanisms of regulation were less intensive in animals that drank water with mineral content of 250 and 500 mg/ℓ; opposite values were demonstrated in the groups given water with extreme levels of mineralization (0 and 1000 mg/ℓ).

Perspiration: Extrarenal elimination of fluid includes excretion in feces, exhaled air, as well as cutaneous perspiration. In our experiment, excretion in feces constituted less than 1% of total fluid turnover, so that we made no adjustment for this route of elimination in our calculations.

Lowest perspiration was observed in animals given water with 500 mg/ℓ minerals. This parameter differed with statistical reliability from the one for all other groups of animals. Maximum perspiration was observed in animals given distilled water. The nature of distribution of this parameter as a function of mineral content of drinking water conformed with the distribution of energy metabolism. The same pattern was retained, according to which the groups of animals next to one another with regard to mineral content of drinking water showed no statistical difference in this parameter; however, with increase in difference in mineral content of water the differences became more marked. The results of indirect and direct measurements were similar with regard to order of the groups as a function of mineralization of drinking water; however, the absolute values for the last tests were 30-40% lower than for the first one, and this also applied to the breadth of distribution between extreme values of the variation series. While in the former case the coefficient of oscillation constituted 35.8%, it was 17.8% in the latter, i.e., the difference between maximum and minimum perspiration was almost twice as great in the first experiment. This fluctuation can apparently be attributed to the fact that direct measurement of perspiration was made in the daytime, when the animals were the least active, since rats are referable to nocturnal animals.

Evaporation is inevitably linked with heat loss, and the organism expends 585 kcal for evaporation of 1 g fluid. We considered it necessary to estimate the aggregate of energy expenditure without heat loss through evaporation, since the latter depended significantly on mineralization of drinking water in our experiment. The confidence interval of this parameter was obtained by estimation [23]. As can be seen in the Table, the reliability of statistical differences between groups was insignificant, and there was virtually no difference between the animals according to calory consumption per unit weight. While the coefficient of oscillation constituted 13% in evaluating overall energy metabolism, the spread constituted 8% when we estimated energy expenditure without perspiration.

As can be seen from the submitted data, the amount of salts in drinking water determines the level of fluid intake to some extent. Water with extreme values for salt content increases fluid intake, which intensifies

not only renal, but extrarenal excretory mechanisms, as a result of which one observes unwarranted (from the standpoint of purposeful behavior) expenditure of energy that was not required by exogenous causes.

On the basis of the foregoing, it can be concluded that the optimum variant, according to the criterion in question, includes water with mineral content of ....[omission in source]; water with mineralization of 100 mg/ℓ is in an intermediate position, but closer to the optimum range.

BIBLIOGRAPHY

1. El'piner, L. I. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1971, pp 73-77.

2. Chizhov, S. V., and Sinyak, Yu. Ye. "Water Provisions for Spacecraft Crews," Moscow, 1972.

3. Shikina, M. I.; Chizhov, S. V.; Krasnoshchekov, V. V.; et al. KOSMICHESKAYA BIOL., No 2, 1971, pp 28-31.

4. Rakhmanin, Yu. A.; Bokina, A. I.; Plugin, V. P.; et al. GIG. I SAN. [Hygiene and Sanitation], No 7, 1975, pp 16-22.

5. El'piner, L. I.; Bokina, A. I.; and Shafirov, Yu. B. Ibid, No 6, 1969, pp 22-26.

6. El'piner, L. I., and Shafirov, Yu. B. Ibid, No 10, pp 19-25.

7. El'piner, L. I.; Shafirov, Yu. B.; and Khovakh, I. M. in "Vsesoyuznaya konf. po gigiyene vody i sanitarnoy okhrane vodoyemov. Materialy" [Proceedings of All-Union Conference on Hygiene of Water and Sanitary Protection of Reservoirs], Moscow, 1969, pp 64-66.

8. Cherkinskiy, S. N. GIG. I SAN., No 8, 1977, pp 3-8.

9. Bokina, A. I. "Physiological Bases of Setting Hygienic Standards for Salt Content of Drinking Water," author abstract of doctoral dissertation, Moscow, 1968.

10. Bokina, A. I.; Fadeyeva, V. K.; and Vikhorva, Ye. M. GIG. I SAN., No 11, 1975, pp 14-19.

11. Shafirov, Yu. B. in "Mezhdunarodnyy simpozium po morskoy meditsine" [International Symposium on Naval Medicine], 7th, summaries of papers, Moscow, 1976, pp 80-81.

12. Rashevskiy, N. in "Teoreticheskaya i matematicheskaya biologiya" [Theoretical and Mathematical Biology], Moscow, 1968, pp 48-66.

13. Antomonov, Yu. G. "Modeling of Biological Systems. Manual," Kiev, 1977.

14. Leninger, A. "Biochemistry," Moscow, 1976.

15. Rozen, R. "Optimality Principle in Biology," Moscow, 1969.

16. Boltyanskiy, V. G. "Mathematical Methods of Optimum Control," Moscow, 1966.

17. Slonim, A. D. "The Environment and Behavior," Leningrad, 1976.

18. Nikolayev, L. A. "Fundamentals of Physical Chemistry of Biological Processes," Moscow, 2d edition, 1976.

19. Schuck, O. "Clinical Nephrology and Pathology of Fluid and Electrolyte Metabolism," Prague, 1970.

20. Paley, P. N.; El'piner, L. I.; Novikova, Yu. P.; et al. in "Gigiyena truda i byta na promyslovykh sudakh v Zapolyar'ye" [Industrial and General Hygiene Aboard Fishing Vessels in the Polar Region], Moscow, 1967, pp 87-105.

21. Todorov, Y. "Clinical Laboratory Tests in Pediatrics," Sofiya, 3d edition, 1961.

22. Verkhin, Ye. B., and Ivanov, Yu. I. "Methods of Experimental Examination of the Kidneys and Fluid-Electrolyte Metabolism," Barnaul, 1972.

23. Urbakh, V. Yu. "Statistical Analysis in Biological and Medical Research," Moscow, 1975.

UDC: 612.233:547.284.3]:313.155

EFFECTS OF DIFFERENT HYGIENIC FACTORS ON EXHALATION OF ACETONE BY MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 77-80

[Article by V. P. Savina and T. I. Kuznetsova, submitted 3 Feb 79]

[English abstract from source]

[Text] Acetone is consistently demonstrated in the atmosphere of pressure chambers. The level thereof changes over a rather wide range, and it depends on conditions of vital functions. For this reason, acetone is a constant factor in airtight spaces, and it is a pressing task to study the patterns of its emission.

Man emits acetone with exhaled air, and together with acetoacetic and β-hydroxybutyric acid, it makes up the group of so-called ketone bodies. The level thereof in blood is determined by the course of reactions of carbohydrate and fatty acid metabolism. The intensity of emission of acetone is related to its level in blood. There is a correlation between acetone levels in blood and exhaled air [1].

Prolonged and considerable stimulation of the sympathetic nervous system, starvation and heavy physical labor lead to intensive formation of ketone bodies in the liver [2]. Moreover, special studies of volunteers revealed that the concentration of acetone in exhaled air increases by over 300 times after a prolonged (20 days) fast.[3]. An increase in emission of acetone is observed not only in the case of total fast, but partial abstinence from food [4]. Acetone is eliminated from the body in exhaled air, urine and perspiration. Living conditions have a substantial effect on human elimination of volatile metabolites.

Acetone was identified in the gas environment of the Skylab orbital station and Soyuz spacecraft. According to data of American researchers, the concentration of acetone in the atmosphere of Skylab-4 was in the range of

6.5-18.7 mg/m^3 at different stages of the mission [5]. The concentration of acetone in the atmosphere of Soyuz-22 was in the range of 5.2-7.8 mg/m^3 [6].

We submit here the results of a study dealing with determination of the effects of exercise ["physical load"], high temperature, humidity and concentration of acetone in the ambient environment, as well as a set of other adverse factors inherent in airtight spaces, on the amount of trace impurities eliminated in exhaled air.

Methods

The air exhaled by subjects and the atmosphere of the pressure chamber was analyzed by the gas chromatographic method using a Varian-Aerograph chromatograph and analytical methods that are in general use in sanitation and industrial chemistry. The obtained data were submitted to statistical processing by the method of Student.

Results and Discussion

We determined the effect of high temperature on quantitative characteristics of metabolites eliminated in exhaled air by the subjects in a series of 3-day tests. Table 1 shows that the concentration of acetone in exhaled air increased by 6.9 times at an ambient temperature of 32-35°C and by 11 times at at a temperature of 40°C, as compared to the background period.

Table 1. Acetone content of atmosphere air exhaled by subjects exposed to high temperature and humidity

Microclimate conditions	Pressure chamber atmosphere, mg/m^3	Exhaled air, mg/m^3
20±2°C	0.1	0.26±0.12
32-35°C, relative humidity 90%	0.89	1.80±0.60
40°C, relative humidity 90%	0.98	2.90±1.40

A significant increase in emission of acetone in exhaled air was recorded during graded exercise on a bicycle ergometer (intensity 800 kg-m/min). Thus, before exercising, the subjects eliminated a mean of 0.99±0.23 mg/h acetone in exhaled air, during exercise the figure was 4.00±0.38 mg/h, immediately after exercising it was 2.72±0.50 mg/h and 1 h after exercise it was 1.09±0.26 mg/h.

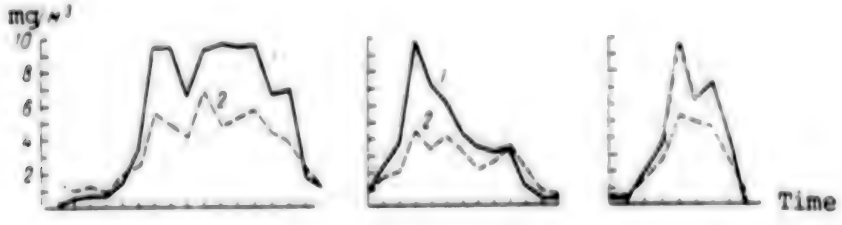
We tested the effect of high acetone concentration in the air environment (8±2 mg/m^3) under different microclimate conditions in a two-compartment pressure chamber 24 m^3 in size. We conducted two 30-day tests on 4 subjects (men 20-30 years of age) in each. Work and rest schedule was the same, and provided for 8 h of sleep and 1 h of rest after lunch. Their food consisted of the onboard rations having 2900-3000 kcal.

For the subjects in this series of studies, we calculated the absolute level of elimination of toxic impurities in exhaled air while in the pressure chamber, under normal microclimate conditions. We used the pulmonary ventilation value, which constituted a mean of 6.97 m^3/day in this group (65 readings) in our calculations. We found that, under normal conditions, a man eliminates 16.1±1.2 mg/day acetone in exhaled air.

Table 2. Elimination of toxic impurities in exhaled air under the influence of acetone for 2 days as related to different ambient temperatures and humidity

Exhaled impurities	t 20±2 C, φ 30–70%		t 35±1 C, φ 40%		t 41±1 C, φ 90%	
	without acetone	acetone, 8 2 mg/m³	without acetone	acetone, 8 2 mg/m³	without acetone	acetone, 8 2 mg/m³
Carbon dioxide	49.6±1.07	50.2±0.31	49.30±1.02	53.3±2.0	50.6±1.5	54.3±4.7
Ammonia	0.94±0.06	1.36±0.11	0.5±0.15	0.80±0.11	1.4±0.21	1.99±0.12
Acetone	18.7±4.3	61.0±1.74	9.0±0.43	55.9±10.0	8.2±1.39	48.2±1.0
Acetaldehyde	1.8±0.12	3.45±0.17	0.6±0.13	3.94±0.81	0.2±0.06	2.5±0.9
Methanol	7.70±0.68	14.40±0.64	2.08±0.61	—	17.10±0.95	6.59±0.51
Ethanol	7.70±1.54	10.90±1.5	31.4±6.4	23.60±4.55	13.2±1.9	20.15±1.42
Fatty acids	6.49±1.56	9.44±1.73	8.69±2.24	10.06±1.67	8.69±0.80	10.81±1.80

Key: t) temperature φ) relative humidity



Acetone content of pressure chamber atmosphere (1) and exhaled air (2). X-axis, time (each graduation corresponds to 2 h)

The obtained data are submitted in Table 2 and the Figure.

As can be seen in the Figure, the concentration of acetone was higher in the pressure chamber than exhaled air. Consequently, when there is a high level of acetone in the atmopshere of the chamber, some is retained in the human body. The difference between acetone content of inhaled and exhaled air constituted 2-4 mg/m^3 for all subjects in all cases. In the case of low concentrations of acetone in the atmosphere this was not observed.

In analyzing the obtained data, we noticed that an increase in concentration of acetone in the atmosphere of the pressure chamber influences the levels of other toxic micro-impurities in exhaled air. Thus, there was an increase in concentration of ammonia and fatty acids in exhaled air during the periods of increased acetone content in the atmosphere of the chamber. There was some decrease in elimination of acetaldehyde at all stages of the study. The changes in amounts of alcohols and carbon dioxide eliminated in exhaled

air were not in the same direction. Thus, under normal microclimate conditions and with high acetone content in the atmosphere, there was almost 2-fold increase in elimination of methanol and 1.5-fold increase in emission of ethanol. During the periods of elevated temperature and humidity, with acetone concentration of 8±2 mg/m^3, we observed a 2.5-fold decrease in elimination of methanol and 1.5-fold increase in that of ethanol.

It should also be noted that with lowering of concentration of acetone in the ambient environment to the base level, a decrease occurs in its concentration in exhaled air, down to normal level, within 1.5-2 h.

BIBLIOGRAPHY

1. Kustov, V. V., and Tiunov, L. A. "Toxicology of Products of Vital Functions and Their Significance in Forming the Artificial Atmosphere of Airtight Spaces," Moscow, 1969, pp 10-15.

2. Ado, A. D., and Ishimova, L. M. (editors) "Pathological Physiology," Moscow, 1973.

3. Savina, V. P.; Stepanov, A. N.; Sokolov, N. L.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1972, pp 67-69.

4. Sargent, F.; Johnson, R.; Robbins, E.; et al. QUART. J. EXP. PHYSIOL., Vol 43, 1958, p 345.

5. Liebich, H.; Bertsch, W.; Zlatkis, A.; et al. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 1002-1007.

6. Savina, V. P.; Mikos, K. N.; Ryzhkova, V. Ye.; et al. KOSMICHESKAYA BIOL., No 6, 1978, pp 18-20.

UDC: 616.68-001.29-003.93-092.9

LESION TO AND RECOVERY OF MOUSE SEMINIFEROUS EPITHELIUM AFTER EXPOSURE TO RADIATION AT DIFFERENT DOSE RATES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 80-83

[Article by Zh. G. Zalikina, submitted 24 Jan 78]

[English abstract from source]

Mice were irradiated with doses varying from 5 to 1200 R at dose rates of 300, 100, 10 and 2.5 R/day. In addition, mice irradiated with a dose of 300 R at dose rates of 300 and 100 R/day were followed up for 3 months. The relationship between gonad injury and the total dosage in the dose range of 5 to 75 R was demonstrated. With an increase in the irradiation time, the effect was dependent on the dose rate.

[Text] Previous studies demonstrated attenuation of the deleterious effect with reduction of radiation dose rate [1-7].

Our objective here was to define the patterns of damage to the seminiferous epithelium in the course of long-term and chronic irradiation, as well as the distinctions of recovery of this tissue after discontinuing exposure to radiation.

Methods

Experiments were conducted on 470 male adult CBA mice (7 animals per group). Radiation was delivered from γ-units with Ce 137, continuously for 22 h a day at dose rates of 300 and 100 R/day (prolonged exposure), 10 and 2.5 R/day (chronic exposure) to cumulative doses of 5 to 1200 R. We studied the radiation damage to the gonads for 3 months after irradiation, for which purpose we used the method of counting cellular elements of the convoluted seminiferous tubules at the 6th and 9th phases of the cell cycle. We estimated the mean number of type B spermatogonia per tubule, as well as other cells of the seminiferous epithelium: spermatocytes, spermatids and spermatozoa. We used cytophotometry to assay RNA in the nucleoli of Sertoli and Leydig cells. We counted the cellular elements and evaluated cytophotometric data in 60 transversely cut tubules.

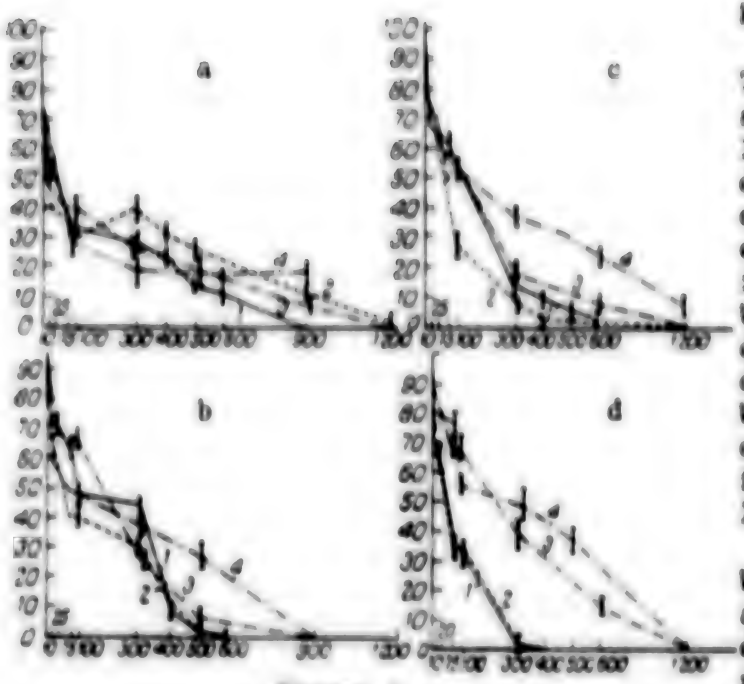


Figure 1.
Cell content of seminiferous epithelium of mice exposed to radiation at different dose rates. Here and in Figure 2: x-axis, cumulative dose (R); y-axis, number of cells (% of control level).
a) spermatogonia c) spermatids
b) spermatocytes d) spermatozoa
1-4) dose rates: 300, 100, 10 and 2.5 R/day, respectively

Results and Discussion

The qualitative changes in seminiferous tissue were similar under all irradiation conditions. There was impairment of topographic arrangement of epithelial cells and thickening of basement membranes. With accretion of radiation dose there was appearance of degenerative and giant cells. With doses of 900-1200 R, only cells of degenerative forms remained in the convoluted seminiferous tubules.

With doses of 5-75 R, there was a distinct correlation between degree of cell damage and radiation dose (Figure 1). In the dose range of 100-400 R, this correlation was less marked. With doses of 500-1200 R, there was a drastic decrease in number of all cellular elements of convoluted seminiferous tubules (conforming with increase in cumulative dose). Under all experimental conditions, a dosage of 5 R elicited visible impairment of spermatogenesis (Figure 2).

We found the dynamics of number of type B spermatogonia interesting (see Figure 1a) with delivery of radiation at the rate of 2.5 R/day. We failed to find doses that would lead to emptying of convoluted seminiferous tubules.

With extended irradiation, spermatozoa disappeared from the convoluted tubules with a dose of 300 R, and in the case of chronic exposure this happened with a dose of 900 R. A 50% decrease in number of spermatozoa was observed in the former case in the dose range of 30-50 R, and in the latter case with doses of 225-300 R.

The low RNA content of Leydig's cells and lesser capacity thereof to synthesize testosterone correspond to slight depression of the cell population in the dose range of 5 to 75 R. Against the background of subsequent increase in RNA synthesis in Leydig's cells, there was gradual depletion of

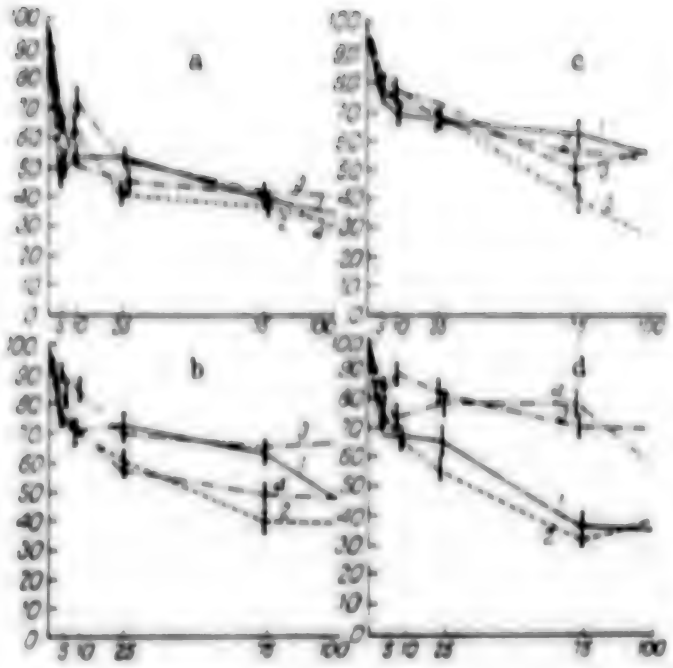


Figure 2.
Damage to seminiferous epithelial cells after delivery of cumulative radiation doses of 5 to 75 R to rats at different dose rates

convoluted tubules. The fluctuation in RNA synthesis in the nucleoli of Sertoli's cells (cells that exchange RNA with spermatocytes and spermatids) showed less correlation with the dynamics of cell population in the seminiferous epithelium. However, the high level of RNA synthesis by these cells warrants the assumption that it is possible for spermatogenesis to be restored with higher accreted doses as well.

The dynamics of number of cell elements in the seminiferous epithelium over a period of 3 months after delivery of 200 R radiation at dose rates of 100 and 300 R/day were similar with both dose rates. Death and discontinuation of mitosis of type B spermatogonia occurred against a background of peak activity of Leydig's cells and diminished RNA synthesis by Sertoli's cells. Then, against the background of diminished activity of Leydig's cells and increased synthesis of RNA in Sertoli's cells, intensive recovery of the cells of the seminiferous epithelium began. By the 60th postradiation day, the undulant fluctuations of intensity of RNA synthesis in the nucleoli of Sertoli's and Leydig's cells stop, and RNA content was close to the control level. After irradiation, the type B spermatogonia content of seminiferous tubules constituted 57% of the control level. Degeneration of spermatogonia type B played an insignificant role in the course of disappearance of these cells. One day after the start of irradiation, the stages of type B spermatogonia reach the intermediate type, and after 3 days they reach the A_4 type, if we consider that the effect of radiation in doses of 100-300 R leads to delay in spermatogonial mitosis in the 6th-8th h [8, 10, 11]. Hence, if type A_4 and intermediate spermatogonia have reached stage B in sufficient number, their radiosensitivity is the same, rather than different as previously assumed [9, 12]. There was a minimal number of type B spermatogonia, 3% of the control level 8 days after irradiation. This time coincides with development of type B spermatogonia from A_0. Evidently, initiation of differentiation of stem cells is the most radiosensitive process, depression of which under the influence of radiation leads to disappearance of the spermatogonial population. The change in number of spermatocytes, spermatids and spermatozoa was similar to the change in number of spermatogonia, occurring within the intervals required for development of these

cells from stem cells. If the decrease in number of spermatogonia, for example, of the B type were the only cause of disappearance of the other cells, they should have been present in the seminiferous tubules in the normal amount. However, their number diminished considerably sooner than the normal time. Consequently, we are dealing with immediate radiation-induced death of these cells. Initiation of differentiation of sex cells from stem cells is the most radiosensitive process. Evidently, temporary discontinuation of spermatogonial mitoses is the chief cause of depletion of the tubules.

It should also be noted that recovery of type B spermatogonia was related to radiation dose rate: it occurred faster and was more complete after a dose rate of 300 R/day than 100 R/day.

Thus, we demonstrated that the severity of damage to the seminiferous epithelium is a function of radiation dose and dose rate. With accretion of radiation dosage there was an increase in damage to germinative tissue, but this function was not linear. A predominant influence of radiation dosage on processes of injury was noted during the first days of prolonged and chronic irradiation. With increase in exposure time, the radiation dose rate became the decisive factor in processes of damage to germinative tissue.

BIBLIOGRAPHY

1. Zalikina, Zh. G. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, Vyp 2, 1975, p 71.

2. Keyzer, S. A., et al. in "Konferentsiya po radiatsionnoy gigiyene. Trudy" [Proceedings of Conference on Radiation Hygiene], Leningrad, 1960, p 154.

3. Keyzer, S. A., and Zavalishina, O. A. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences. Biology Series], No 5, 1965, p 780.

4. Keyzer, S. A. in "Vsesoyuznyy s"yezd rentgenologov i radiologov. 8-y. Trudy" [Proceedings of 8th All-Union Congress of Roentgenologists and Radiologists], Moscow, 1966, p 673.

5. Keyzer, S. A., and Lemash, G. A. VESTN. AMN SSSR [Vestnik of the USSR Academy of Medical Sciences], No 12, 1967, p 53.

6. Plakhuta-Plakutina, G. I., et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1972, p 29.

7. Savina, Ye. A., et al. in "Voprosy radiobiologii i biologicheskogo deystviya tsitostaticheskikh preparatov" [Problems of Radiobiology and Biological Effects of Cytostatic Agents], Tomsk, Vol 5, 1973, p 49.

8. Canti, R. G., and Spear, F. J. PROC. ROY. SOC. B., Vol 105, 1929, p 93.

9. Clow, D. W., and Gillette, E. L. RADIAT. RES., Vol 42, 1970, p 397.

10. Henshaw, P. S. AM. J. ROENTGENOL., Vol 27, 1932, p 890.

11. Idem, RADIOLOGY, Vol 49, 1947, p 349.

12. Oakberg, E. F. J. EXP. ZOOL., Vol 134, 1957, p 343.

UDC: 612.014.43-085.23

THE ROLE OF TEMPERATURE IN EXPERIMENTS ON BIOLOGICAL OBJECTS UNDER EXTREME CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 83-85

[Article by F. V. Sushkov and T. M. Smirnova, submitted 26 Jun 78]

[Text] Not infrequently, experiments dealing with the effects of extreme factors on processes in biological objects that do not have a system of heat regulation, which is inherent in homoiothermic animals are conducted without monitoring ambient temperature. Temperature fluctuations could be the cause of many changes. We submit here the results of analysis of experimental data obtained from culturing mammalian cells at different temperatures.

Methods

We studied 8 cell lines obtained from different human and animal organs (see Table). BHK-21 [baby hamster kidney], Wish, 237 and 451 cell lines were cultured in Eagle's medium and the others in medium 199 with addition of 10% bovine serum and antibiotics. The cultures were incubated at temperatures of 28-36°C, and some lines were incubated at 39, 41 and 42°C. We determined the duration of mitosis (T_m) using the stathmokinetic (colchicine) method [1] in the middle of the phase of logarithmic growth. All of the figures cited here are the results of at least 10 readings.

Results and Discussion

The Table clearly demonstrates that T_m is a function of ambient temperature. As shown by our estimates, this function is governed by the law of Arrhenius, according to which it has the following appearance:

$$T_m = \exp(A + E_a RT),$$

where E_a is energy of activation, T is absolute temperature and R is the Boltzmann's gas constant.

Duration of cell mitosis (T_m, min), energy of activation (E_a) and temperature coefficient (Q_{10})

Cell line index	Source	Mitosis time, min					E_a	Q_{10}
		28	30	32	34	36		
L	Mouse subcutaneous tissue	132±3.8	117±4.7	90±7.6	79±4.2	46±2.5	24	3.3
BHK-21	Syrian hamster kidney	127±4.1	106±2.2	79±2.8	63±3.0	49±1.9	24	3.3
237	Sublines of Chinese hamster connective tissue cells	120±11.1	99±7.7	70±3.8	57±3.9	47±3.7	24	3.3
451		169±10.3	116±4.3	85±3.3	—	49±3.0	30	4.6
MK-2	Monkey kidney	∞	163±10.3	126±9.8	—	72±3.5	27	3.9
RH	Human kidney			∞	101±6.0	67±3.5	40	—
Hep-2	Human laryngeal carcinoma	∞	177±17.2	127±7.3	—	56±3.9	38	—
Wish	Human amnion				116±14.2	67±4.2	54	—
A-1	Same	148±9.4	—	—	—	83±5.5	29	4.2

Note: The symbol ∞ refers to temperatures at which T_m is so long that it is not demonstrable by the colchicine method.

Figure 1 clearly illustrates that T_m is an exponential function of temperature; it shows the lines of regression of T_m for 237, Wish and 451 cells. E_a was determined from these lines using the least squares method. The obtained values of E_a and calculated values of Q_{10} are listed in the Table.

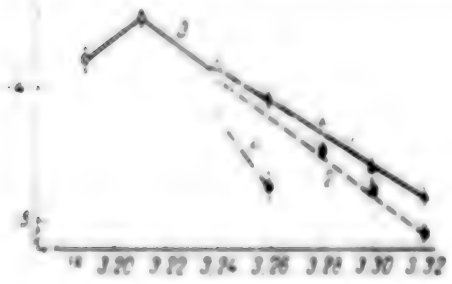


Figure 1.
Lines of regression of T_m for Chinese hamster (237 and 451) and Wish cells. Here and in Figure 2: x-axis, value of $10^3/T$; y-axis, natural logarithm of mitotic rate.
1 and 2) 237 and 451 cells, respectively, at 28-36°C
3 and 4) 237 and Wish cells at 36-42°C

Studies of temperature dependence of a number of biological processes in protozoans and animal cells over a wide range of temperatures revealed several salient points on Arrhenius' curve [2-4]. Since we did not obtain an appreciable salient point ["break"] on the curves of regression of T_m at the tested temperatures, we conducted a second series of experiments cultivating L and 237 cells at 36, 39, 41 and 42°C. We found that these cells reacted differently to temperature elevation.

T_m of Chinese hamster cells in this series of experiments constituted 50±2.2 min at 36°C. T_m decreased to 33±1.9 min at 39°C and ranged from 35 to 72 min (M±m = 46±3.6) in different experiments at 41°C.

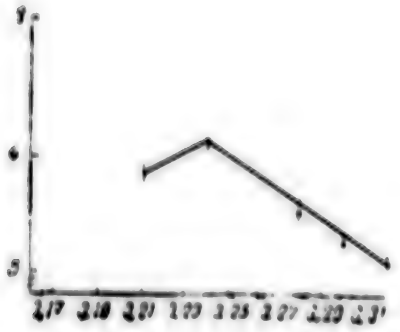


Figure 2.
Arrhenius curves for L cells

Consequently, the exponential nature of T_m as a function of temperature was retained in 237 cells in the temperature range of 28-39°C. A temperature of 41°C is critical, and with it there is an abrupt break in the regression line (see Figure 1). At 41°C or higher, the rule of Arrhenius does not apply, and T_m increases with increase in temperature. At 42°C, we were able to determine mitosis time only on the 1st day of incubation (it constituted 2 h or more). At later stages there was development of marked degeneration of cells. In the L cell culture, the described phenomena developed at lower temperatures. Already at 39°C, T_m increased drastically, as compared to 36°C, constituting 72±6.4 min, whereas virtually no mitoses were demonstrable at 41°C. There was distinct degeneration of cells already on the 1st day of incubation. Thus, 39°C is the top critical temperature for L cells (Figure 2).

In the HeLa culture, T_m as a function of temperature was governed by the law of Arrhenius at 29-38°C, while 40°C was the critical point, at which this pattern was impaired. Instead of exponential decrease, there was a drastic increase of T_m [5]. Thus, there was distinct manifestation of dissimilar reactions of different cell lines to the same temperatures, as we showed for three types of cell cultures. These data indicate that relatively minor (within 2°C) changes in temperature led to substantial cytophysiological changes.

The changes in temperature compatible with mitosis in the direction of elevation led to rapid death of cells, as demonstrated in our studies of L cells at 41°C and Chinese hamster cells at 42°C. A decline of temperature beyond this range was not as devastating, but induced persistent and profound changes in structural organization and the genetic system of cells [6].

Thus, in experiments with "poikilothermic" biological objects under uncontrolled conditions, the changes induced by temperature fluctuations could be more substantial than those due to the influence of tested factors (for example, weightlessness, steady magnetic fields, etc.). The demonstrated changes could be erroneously attributed to effects that develop from studied conditions. This was clearly demonstrated in experiments with plants [7, 8].

Our experimental data, on the example of one cytophysiological parameter, clearly demonstrate the need for strict control of ambient temperature when studying the effects of extreme factors on isolated mammalian cells and populations of freely living organisms that have no heat-regulating systems.

BIBLIOGRAPHY

1. Zosimovskaya, A. I., and Lyapunova, N. A. TSITOLOGIYA [Cytology], No 2, 1966, pp 208-215.

2. Drost-Hansen,W. ANN. N.Y. ACAD. SCI., Vol 125, 1965, pp 471-501.

3. Lau, L. EXP. CELL RES., Vol 71, 1972, pp 475-477.

4. Idem, Ibid, Vol 73, pp 523-525.

5. Rao, P., and Engelberg, J. in "Cell Synchrony, Studies in Biosynthetic Regulation," New York, 1966, pp 332-352.

6. Hampel, K., and Lewan, A. HEREDITAS (Lund), Vol 51, 1964, pp 315-343.

7. Platonova, R. N.; Ol'khovenko, V. P.; Parfenov, G.P.; et al. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 6, 1976, pp 903-913.

8. Platonova, R. N.; Ol'khovenko, V. P.; Parfenov, G. P.; et al. Ibid, No 1, 1977, pp 65-72.

BRIEF REPORTS

UDC: 611-18.46:629.78

MICRONUCLEI IN RAT BONE MARROW AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 85-87

[Article by T. P. Pantev, G. N. Durnova, I. I. Britvan, I. T. Nikolov and S. Ts. Topalova, submitted 16 Nov 78]

[Text] It is known that during space flights such factors as weightlessness, accelerations, hypodynamia, noise, vibration, ionizing radiation, etc., affect man and animals. In spite of the many space studies conducted with different biological objects, not enough information has been gathered on the effects of weightlessness on physiology of the organism as a whole and individual cells thereof in particular; no quantitative or qualitative characteristics have been obtained of processes that take place on the cellular and subcellular levels. In order to assure the safety of space flights, it is also necessary to assess the effects of extreme factors associated with space flights on genetic structures of cells [1-3].

We have made an attempt here to evaluate the chromosomal system of the rat's somatic cells during exposure to weightlessness, artificial gravity and other flight factors using the so-called micronuclear test. This method of assessing the mutagenic effects of different factors is based on determination of the number of fragments of damaged chromosomes which, being deprived of a centromere, remain in the anaphase. Fragments of damaged chromosomes are counted in the interphase when, being contained in the cytoplasm of daughter cells, they remain in the form of one or several secondary nuclei that are considerably smaller in size than true nuclei. The micronuclear test was proposed as a means of obtaining speedy [express] information about chromosomal damage almost simultaneously in several works [4-8], for both bone marrow cells and erythrocytes. The micronuclear test has several advantages over the usual metaphase methods, due to its simplicity and speed of counting [6, 9].

We counted the karyocytes with micronuclei (MN) in the bone marrow of rats flown aboard Cosmos-936 biosatellite within the first few hours after landing and after 25 days of readaptation to living conditions on the ground.

Methods

Bone marrow from the humeral and iliac bones of male, Wistar albino rats free of pathogenic microflora served as the material under study. We examined 15 rats flown aboard the Cosmos-936 biosatellite (18.5 days), 10 of which were in weightlessness throughout the flight (FW_2 and FW_3 groups), while 5 were rotated on a centrifuge (FC_2 group). Bone marrow of 10 rats in the ground-based model experiment (SW_2 and SW_3 groups), as well as bone marrow from 18 intact rats in the vivarium control (VC_0, VC_2 and VC_3 groups) served as a control. The material was collected for examination 11-13 h (FW_2, SW_2 and VC_2 groups) and 25 days (FW_3, CW_3, FC_2 and VC_3 groups) after the flight and ground-based experiments. We took bone marrow from group VC_0 rats (preflight vivarium control) several days prior to launching the biosatellite. The conditions under which the experiment was conducted aboard Cosmos-936 were described in detail elsewhere [10].

We counted the karyocytes with MN in the bone marrow of humeral and iliac bones by the method of Heddle [7]. We submitted to analysis 2000 bone marrow cells from each animal. The results were submitted to statistical processing by the methods of variational analysis using the χ^2 criterion [11, 12]. Differences between the control and experiment were considered reliable with $P \leq 0.01$).

Results and Discussion

As can be seen from the data listed in Table 1, the set of factors involved in the flight and ground-based model experiments elicited distinct changes in the chromosomal system of bone marrow cells of experimental animals. There was a 7-8-fold increase in percentage of cells with MN in animals that were in weightlessness during the space flight (FW_2 group), and a 5-fold increase in those in the ground-based model experiment (SW_2), as compared to the vivarium control (VC_0 and VC_2). The absence of statistical differences in incidence of appearance of cells with MN in the bone marrow of rats submitted to weightlessness and rats in the ground-based experiment warrants the assumption that the aggregate of unusual living conditions (hypodynamia, isolation, gas environment, etc.), rather than absence of gravity, was the cause of the demonstrated changes.

No differences in parameters were demonstrated between the experimental and control groups after the 25-day period of readaptation (Table 2). It must be noted that the variations in number of cells with MN in some animals were considerably greater 25 days after the flight and ground-based experiments than in the first few hours after terminating them (see Figure).

It is known that rats are quite active animals. Keeping them in small cages that restricted their mobility, as well as the other unusual conditions associated with the space flight, could apparently cause development of a stress reaction capable of altering the hormone balance [13, 14] and influencing the genetic system of hemopoietic tissue [13], hemopoietic activity [15] and a number of other physiological functions. Subsequent

readaptation of the rats to earth's conditions was an equally potent stressor. Although, theoretically, we could have assumed that changes could occur in the genetic system of somatic cells under the influence of weightlessness [2, 3], our findings indicated that weightlessness during the flight aboard the biosatellite did not elicit an increase in chromosomal aberrations. The findings are quite consistent with data to the effect that no cytogenetic changes were present in peripheral blood lymphocytes of the crews of Soyuz-3, 6-9, 13 and 17 spacecraft [1, 16]. On the other hand, it should be noted that examination of the crews of the American spacecraft, Gemini [16], Apollo [16, 17] and Skylab [18] revealed an increase in incidence of chromosomal aberrations in peripheral blood lymphocytes.

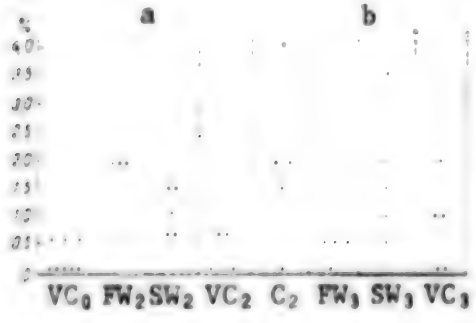
Table 1. Number of cells with MN in humeral bone marrow 11-13 h after termination of experiment (M±m)

Animal group	Number of rats	Number of cells examined	Cells with MN, %
Preflight vivarium control (VC_0)	8	1.6×10	0.19±0.07
Weightlessness (FW_2)	5	10^4	1.50±0.32
Ground-based model experiment (SW_2)	5	10^4	1.00±0.21
Vivarium control (VC_2)	5	10^4	0.20±0.11

Note: $P\leq0.01$ when we compared the following groups: VW_2--VC_0, SW_2--VC_0, VC_2--FW_2, VC_2--SW_2

Table 2. Number of cells with MN in iliac bone marrow 25 days after termination of experiment (M±m)

Experiment	Number of rats	Cells examined	Cells with MN, %
Weightlessness + centrifuge (accelerations 1 G) (FC_2)	5	10^4	1.90±0.86
Weightlessness (FW_3)	5	10^4	0.60±0.32
Ground-based model experiment (CW_3)	5	10^4	1.70±0.64
Vivarium control (VC_3)	5	10^4	0.50±0.28



←Number of cells with MN in bone marrow of different animals

The results of our study enable us to derive the following conclusions: a) exposure of animals to space flight conditions and the ground-based model experiment leads to damage of the chromosomal system of nuclear cells of bone marrow; b) weightlessness for 18.5 days did not elicit significant damage to the

chromosomal system of bone marrow cells; c) the demonstrated changes in the chromosomal system were reversible, and they had a tendency to revert to normal after a 25-day period of readaptation.

BIBLIOGRAPHY

1. Bobkova, N. N., and Krupina, T. N. GENETIKA [Genetics], No 9, 1975, pp 145-150.

2. Kondo, S. JAP. J. GENET., Vol 43, 1968, pp 467-481.

3. Pollard, E. C. J. THEORET. BIOL., Vol 8, 1965, pp 113-131.

4. Matter, R. C., and Schmid, W. MUTAT. RES., Vol 12, 1971, pp 417-425.

5. Schmid, W. AGENTS AND ACTION, Vol 3, 1973, pp 77-85.

6. VonLedebur, M., and Schmid, W. MUTAT. RES., Vol 19, 1973, pp 109-117.

7. Heddle, J. A. Ibid, Vol 18, pp 187-190.

8. Miller, R. C. ENVIRONM. HLTH. PERSPECT., Vol 6, 1973, pp 167-170.

9. Chaubey, R. C.; George, K. P.; and Sundarm, K. in "Symposium on Structural and Functional Aspects of Chromosomes. Proceedings," Bombay, 1975, pp 205-222.

10. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1979, pp 18-22.

11. Rokitskiy, P. F. "Biological Statistics," Minsk, 1964.

12. Strelkov, R. B. "Method of Calculating Standard Error and Confidence Intervals of Arithmetic Means With the Use of a Table," Sukhumi, 1966.

13. Baran'ski, S.; Baran'ska, V.; and Shimkovyak, V. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, p 6.

14. Saksonov, P. P.; Antipov, V. V.; and Davydov, B. I. "Essays on Cosmic Radiobiology," Moscow, 1968.

15. Belkaniya, G. S., and Lapin, B. A. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy," Moscow, 1977, pp 8-9.

16. Bobkova, N. N., and Krupina, T. N. KOSMICHESKAYA BIOL., No 6, 1973, pp 31-35.

17. Gooch, P. C., and Berry, C. A. AEROSPACE MED., Vol 40, 1969, pp 640-642.

18. Shaw, M., and Gooch, P. C. AM. J. HUM. GENET., Vol 22, 1970, pp 11-21.

19. Lockhart, M. in "Skylab Life Sciences Symposium. Proceedings," Houston, 1977, p 29.

UDC: 612.822.3.014.426

ANALYSIS OF CHANGES IN EVOKED BIOELECTRICAL ACTIVITY OF THE BRAIN DURING EXPOSURE TO HIGH-INTENSITY STATIONARY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 88-90

[Article by L. D. Klimovskaya, submitted 9 Nov 78]

[Text] It has been previously shown that a significant increase in amplitude and complication of form of somatosensory evoked potentials (EP) of the cerebral cortex and cerebellum are observed in rats anesthetized with nebutal during exposure to a stationary magnetic field (SMF) [1]. The nature of changes in evoked activity warrants the assumption that an SMF facilitates appearance and propagation of an excitatory process in neuronal ensembles that form the electrical response to an afferent signal. We studied here the possibility of modifying the effect of SMF by means of alterting the functional state of the central nervous system. For this purpose, we used strychnine and high-frequency stimulation of the reticular formation of the midbrain.

Methods

Experiments were conducted on 50 albino rats under nembutal anesthesia (40 mg/kg intraperitoneally). The sciatic nerve was stimulated with single, square-wave pulses lasting 0.5 ms. EP were derived unipolarly using silver or nichrome electrodes from the cerebral cortex, reticular formation of the midbrain and cortex of the anterior vermis of the cerebellum. The reticular formation was stimulated for 30 s through bipolar nichrome electrodes using square-wave pulses lasting 0.1 ms at a frequency of 300 pulses per second at a voltage of 10 V. Localization of electrodes was checked on histological preparations. Strychnine was given intraperitoneally in a subconvulsive dosage of 2.0 mg/kg. In this study we used an SP-15A electromagnet with flat parallel tips 300×400 mm in size; the south pole of the magnet was on the top tip. The magnetic field was virtually homogeneous in the central part of the interpole space in an area of 300×200 mm, and the decline of intensity in the rest of the space did not exceed 15-20% of the level in the middle. There was 1.8% pulsation of voltage. The rats were immobilized on a stand with the belly down, placed in the opening of the magnet and submitted to vertically directed SMF of 500-4000 Oe. We

recorded the EP of each rat using an oscillograph, before, during and after exposure to SMF.

Results and Discussion

The electrical responses of brain structures to stimulation of the sciatic nerve consisted primarily of biphasic potentials of relatively low amplitude. Amplitude of EP of the sensorimotor cortex, measured from peak to peak, constituted 180.1±19.9 μV, that of the mesencephalic reticular formation was 202.7±17.7 μV and cerebellum 157.1±16.7 μV.

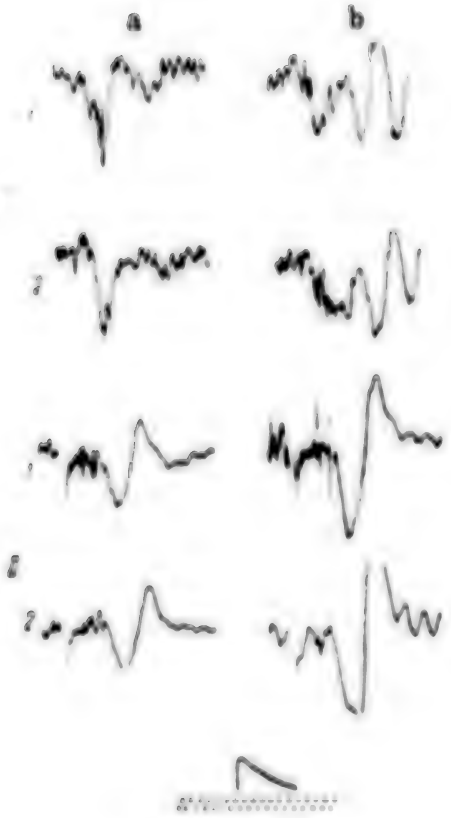


Figure 1.
Changes in cerebellar EP with repeated exposure to SMF of 3000 (I) and 1000 Oe (II).
a) before exposure
b) during exposure to SMF
1,2) first and second exposure
Here and in Figure 3: at the bottom time calibration is 10 ms, and amplification is 50 μV

The effect of SMF on evoked activity of the brain was determined by the intensity of the field and individual sensitivity of the animals. in a 4000-Oe field, most rats presented a 2-3-fold increase in amplitude of EP and appearance of 3-5 additional phases in the structure. The changes in evoked activity were similar in nature in all tested parts of the brain. But, they could arise in different structures of the same animal at different SMF intensities. In most cases, changes in cerebellar EP were demonstrated with lower SMF levels than changes in EP of the cerebral cortex and reticular formation. With repeated exposure to SMF after 20-30 min, there was complete reproduction of the initial effect (Figure 1). According to the mean data (13 rats), SMF of 1000 Oe elicited an increase in amplitude of cerebellar EP to 179.6±15.4% of the base level the first time and to 175.0±16.7% the second time. Studies of evoked activity of other parts of the brain also failed to demonstrate statistically reliable differences between the intensity of reactions to the first and second exposure to SMF. These data enabled us to make a comparison of SMF effects on the same animal before and after giving it strychnine.

In a special series of experiments, we studied the dynamics of changes in evoked activity of the brain for 60 min after intraperitoneal injection of strychnine. Already after 5 min, we could detect an increase in EP. By the

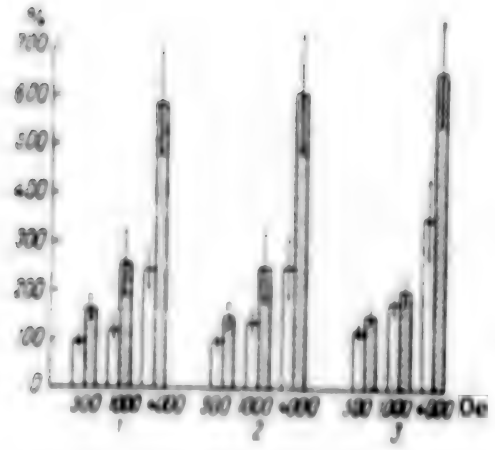


Figure 2.
Influence of preliminary administration of strychnine on effect of SMF. X-axis, field intensity; y-axis, EP amplitude during exposure to SMF (% of base level). White columns--before, striped collumns--after administration of strychnine

10th min, the reaction reached a maximum (2-3-fold increase in amplitude, more complicated form) and held at this level to the 30th min, after which it gradually recovered. The nature of the demonstrated changes was similar to that observed with application of strychnine to the cerebral cortex [2], cerebellar cortex [3], as well as with direct injection into the reticular formation of the mesencephalon [4].

We evaluated the effects of SMF during the period of maximal action of strychnine. At first the rats were exposed to SMF of increasing intensity (500, 1000 and 4000 Oe) for 15 min; then the electromagnet was turned off, strychnine was given and exposure to SMF was repeated after 10 min. The averaged results of these experiments, which were conducted on 20 rats, are illustrated in Figure 2, which clearly shows a significant enhancement of the effect of SMF, as assessed by the degree of increase in amplitude of electrical responses of the brain after administration of strychnine.

The enhancing effect of strychnine on SMF action was also manifested in the changes in form of electrical responses of the brain. It should be noted that there were considerable differences between the changes in EP under the influence of SMF and administration of strychnine. In the former case, the duration of the additional phases was approximately the same as that of the first phase of the primary response (20-30 ms), and the EP sometimes acquired a spindle-like shape; in the latter case, there was enhancement or appearance of spike components, with occasional appearance of very slow ones, the duration of which was considerably longer than that of the primary response. Under the influence of strychnine, there was a substantial intensification of the changes in EP form typical of the effect of magnetic fields.

As we know, strychnine has the capacity of selectively depressing postsynaptic inhibition [5, 6]. Perhaps, blocking of postsynaptic inhibitory processes intensifies the effect of SMF on the functional state of afferent systems of the brain.

Evidently, excitation of the reticular activating system of the brain stem can have an analogous influence. Without dwelling on a description of the distinctions of reticular influences on evoked activity of the brain during exposure to SMF (this was the subject of a special study [7]), let us

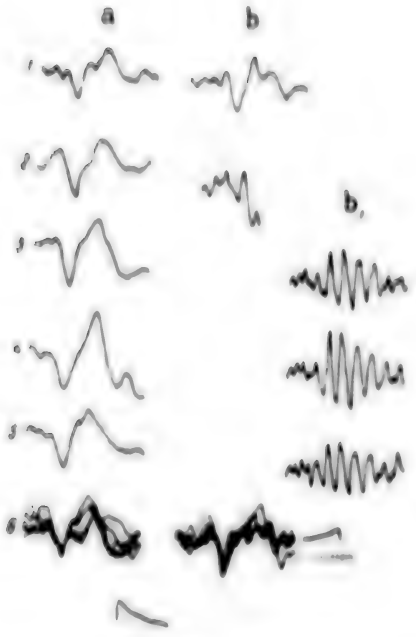


Figure 3.
Changes in EP of cerebellum after stimulation of mesencephalic reticular formation, before and during exposure to 4000-Oe SMF
a) before exposure
b) during exposure to SMF
b1) segment of tracing in SMF with reduced amplification and paper feeding rate
1) before stimulation
2-6) 5, 10, 20, 30 and 60 s, respectively, after stimulation

mention only that we succeeded in demonstrating that it is possible to provoke the effect of a magnetic field by means of high-frequency stimulation of the reticular formation. It is opportune to recall here that stimulation of the reticular formation elicits convulsive discharges in the sensory cortex that has been pretreated with a subthreshold dose of strychnine [8]. A similar situation apparently occurred with exposure to the magnetic field, when the used intensity was insufficient for appearance of marked changes in evoked activity. Exposure to SMF merely prepared the cerebellum for exalted responses, and for appearance thereof an additional factor was required, and the enhancing influences of the reticular formation played this role (Figure 3).

Thus, the effect of SMF can apparently be summated, to some extent, with the excitatory influences of strychnine and the mesencephalic reticular formation. Under these conditions, exaltation of evoked bioelectrcal activity of the brain was significantly intensified, and the nature of the changes was typical of the effect of SMF. In all probability, administration of strychnine and high-frequency stimulation of the mesencephalic reticular formation were instrumental in effectuating the enhancing influences of the magnetic field on circulation of the excitatory processes in neuronal ensembles that form the electrical response to an afferent signal.

BIBLIOGRAPHY

1. Klimovskaya, L. D., and Smirnova, N. P. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 8, 1976, pp 906-910.

2. Roytbak, A. I. "Bioelectrical Phenomena in the Cerebral Cortex," Tbilisi, Pt 1, 1955.

3. Bratus', N. V. "The Cerebellum and Visceroreceptors," Leningrad, 1969.

4. Ryabinina, M. A. ZH. VYSSH. NERVN. DEYAT. [Journal of Higher Nervous Activity], No 4, 1967, pp 697-704.

5. Eccles, J. C. "Physiology of Nerve Cells," Moscow, 1959.

6. Purpura, D. in "Mekhanizm tselogo mozga" [Mechanism of the Entire Brain], Moscow, 1963, pp 9-137.

7. Klimovskaya, L. D. ZH. VYSSH. NERVN. DEYAT., No 1, 1979, pp 196-199.

8. Bremer, F. in "Elektroentsefalograficheskoye issledovaniye vysshey nervnoy deyatel'nosti" [Electroencephalographic Study of Higher Nervous Activity], Moscow, 1962, pp 119-128.

UDC: 612.015.34:547.532]-06:612.766.2

DISTRIBUTION OF BENZENE IN TISSUES OF HYPOKINETIC ANIMALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 90-91

[Article by G. P. Babanov and A. L. Isakhanov, submitted 29 May 78]

[Text] The intensive development of technology, mechanization and automation of modern industry are leading to rapid and significant decrease in man's muscular activity during work. Hypokinesia alters the defense capabilities of the body when it is exposed to various physical, chemical and biological environmental factors. For example, the reaction of man and animals to administration of some pharmacological products changes, and duration of anesthesia increases as a function of duration of hypokinesia [1-3].

One encounters the combined effect on man of hypokinesia and various chemical compounds at chemical plants, in submarines and spacecraft. One cannot rule out the possibility that toxic agents accumulate in the air, both during normal work and in case of accidents (leaks) [4].

It is interesting to know the distribution of chemicals in the organs of hypokinetic animals. We selected one of the representatives of nonelectrolytes, benzene, as the factor affecting the organism.

Methods

We conducted our study on 16 mongrel albino rats divided into 2 groups of 8 animals. To create hypokinesia we placed the animals in special box-cages made of plexiglas for 8 weeks. After this time, rats from the control (usual motor activity) and experimental (hypokinesia) groups were submitted to 4-h inhalation of benzene in a concentration of 18 mg/ℓ (2/3 of Lim_N). After this inhalation, animals in both groups were decapitated. We took tissues of the liver, kidneys, lungs, spleen, adrenals, heart, sternum, femoral muscle, brain, as well as blood, for examination. We placed 400-500 mg of each sample, both adrenals and 1 mℓ blood in airtight centrifuge tubes containing an extracting agent (1 mℓ [omission] and n-nonane), and the tubes were put in a refrigerator for primary extraction. After 24 h the tissues were ground, and the tubes were replaced in the refrigerator for

96 h for complete extraction. Benzene was demonstrated by liquid-gas chromatography on an LKhM-8 MD instrument using a flame-ionization detector. We used copper columns 3000 mm in length and 3 mm in diameter. We used apiezon M as the stationary phase, which was applied in an amount constituting 10% (weight) of the solid phase on cellite-545. The following modes were used: +150°C temperature of evaporator, +135-140°C column temperature and nitrogen (60 ml/min) as the gas carrier. The samples were put in the instrument with an MSh-10 microsyringe. Quantitative assay of benzene was made by the endogenous standard method.

Results and Discussion

It was established that permeability of most tissues was higher for the nonelectrolyte in hypokinetic animals than controls (see Table). In control animals, maximum amounts of benzene were demonstrable in the adrenals, omentum, liver and sternum, and the distribution of benzene in hypokinetic animals was essentially similar to the control. Benzene accumulated the most in the adrenals, although a tendency toward decline was observed, as compared to the control. The liver was in second place, with regard to benzene content; in addition, there was marked increase in accumulation of benzene in the liver, as compared to the control. We were impressed by the greater affinity of brain tissue for benzene in hypokinetic animals, and this tissue was in fourth place with respect to amount of accumulated benzene (7th in the control). Benzene accumulated to a lesser extent in the omentum of experimental animals, which was apparently attributable to the fact that the store of fat in it was rather insignificant, as compared to the control. The increase in benzene content of the liver, brain, blood, sternum, lungs, kidneys and heart of experimental animals was 3.16, 2.18, 2.1, 1.89, 1.88, 1.6 and 1.41 times greater, respectively, than in control animals.

Distribution of benzne (mg% wet tissue) in albino rat organs after inhalation thereof for 4 h in a concentration of 18 mg/l, M±m

Tissue	Control	Hypokinesia	P
Adrenals	91.93±21.27	62.69±6.38	>0.3
Omentum	35.40±7.92	15.83±4.50	<0.01
Liver	17.74±3.97	56.08±11.04	<0.001
Sternum	14.10±1.93	26.64±3.46	<0.02
Kidneys	8.8±0.53	14.10±2.23	<0.001
Heart	8.06±3.49	11.87±4.41	>0.5
Brain	7.89±1.35	17.22±2.62	<0.01
Spleen	5.78±0.62	9.59±3.95	>0.5
Blood	5.54±0.46	11.68±1.65	<0.001
Lungs	5.38±1.0	10.13±3.61	<0.05
Muscle	4.45±0.86	7.01±2.16	>0.5

Thus, prolonged hypokinesia led to an increase in permeability of most tested tissues of experimental animals to benzene, which is a typical nonelectrolyte. The obtained data warrant the belief that hypokinesia leads to an increase in tissular permeability to other "nonreactive" nonelectrolytes also, as well as to faster development of poisoning.

BIBLIOGRAPHY

1. Vasil'yev, P. V., and Lapinskaya, B. Yu. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 206-214.

2. Kustov, V. V., and Tiunov, L. A. "Toxicology of Products of Vital Functions, and Their Significance in Forming the Artificial Atmosphere of Airtight Spaces," Moscow, 1969.

3. Kolemeyeva, L. Ya., and Shashkov, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1974, pp 14-19.

4. Wands, K. R. in "Fundamentals of Space Biology and Medicine," Moscow, Vol 2, Bk 1, 1975, pp 74-104.

BOOK REVIEWS

UDC: 616.831-073.731-073.96(049.32)

NEW BOOK DEALS WITH VELOCITY RHEOENCEPHALOGRAPHY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 pp 91-93

[Review by Kh. Kh. Yarullin of the book: "Skorostnaya reoentsefalografiya" by V. Mitkov and P. Rashkov, Sofia, Medicine and Physical Culture Publishing House, 1978]

[Text] Synchronous recording of rheoencephalograms (REG) and their first derivatives increases significantly the informativeness of impedance methods, since the differential rheogram, which reflects more finely the state of cerebral hemodynamics, permits detection of early atherosclerotic and functional changes in cerebral vessels. However, in spite of the considerable advances in clinical rheoencephalography, the diagnostic capabilities of the first derivative have not been sufficiently explored, and rather limited clinical use is being made of them. For this reason, the publication of this monograph by Bulgarian scientists is quite timely.

The monograph is the result of 12 years of creative work by a clinical neuropathologist and design engineer.

The present status of development of clinical rheoencephalography is described concisely and, at the same time, fully enough. The critically argumented brief survey shows convincingly the predominantly intracranial genesis of REG and the wide possibilities of using it in clinical practice.

Chapter 1 deals with the principles of rheography, its biophysical and clinicophysiological bases. Numerous data from the literature, as well as the authors' own experimental and clinical data, enabled them to derive the following conclusions: the REG is determined primarily by the pulsed oscillations in delivery of blood to the brain; superficial (epidermal) location of electrodes does not hinder obtaining information about the condition of the brain's vascular system; the REG curve records pulsed changes in impedance of the brain and reflects changes in pulsed delivery of blood.

The authors adhere to the opinion that volumetric (classical) and velocity [rate](differential) REG supplement one another. Synchronous recording

of both curves, which have different physical content, yields fuller information about hemodynamics of the brain, which permits deriving better substantiated and more reliable conclusions.

Chapter 2 deals with the equipment and methods of examination. The authors used the M-RG-1 Bulgarian two-channel rheograph designed by P. Rashkov. They used longitudinal hemispheric and regional leads from both sides by the bipolar method and transverse bipolar leads.

The authors stress the need to standardize the unit that provides for electronic differentiation of the rheographic signal. It must permit obtaining a reliable first derivative of the rheographic curve conforming with the physical and mathematical content of this concept, with the accuracy required for practical purposes. As shown by their own experience, a differential system with a time constant of RC = 0.0025 s satisfies these conditions entirely.

Chapters 3 to 9 are the most original and valuable; they deal with analysis of velocity rheograms and the results of their own studies of changes in velocity REG in the presence of vascular and other diseases of the brain.

The authors propose their own method for analysis of velocity rheograms (Chapter 3). Analysis of the literature and generalization of the results of their own studies with the use of the proposed method of analyzing the velocity REG enabled the authors to demonstrate the following advantages: the velocity REG demonstrates a new physical aspect of the process of supplying the brain with blood. The first derivatives of the REG reflect the rate of change in electrical resistance of tissues, which occurs during the pulse cycle, and they indirectly yield information about changes in rate of influx and efflux of blood from the brain; the velocity REG makes it possible to single out new qualitative parameters (moments, time intervals, amplitudes) that enlarge upon and add to information about the state of the cardiovascular system; velocity REG can be used for more accurate read-out of amplitude parameters and time intervals characterizing the volumetric REG; the algebraic relations between some homogeneous parameters defined by the authors on the basis of analysis of velocity curves, which are dimensionless values, change quite graphically with pathological changes in delivery of blood to the brain; with synchronous recording of volumetric and velocity REG's and joint analysis thereof, it becomes possible to make a quantitative evaluation of regional blood flow in the brain; artefacts induced by slow processes (respiratory waves, movement of the subject, certain functional tests) are ruled out in velocity rheographic recordings. Depression of the lowest frequencies of the rheograph's differentiating system makes it possible to obtain tracings of good quality, even when it is impossible to eliminate, on volumetric REG's, respiratory and other artefacts in seriously ill patients with impaired consciousness.

Chapter 3 ends with a description of pathological changes in velocity REG's. Organic changes in cerebral vessels affect not only the shape, but different parameters of velocity REG's.

Velocity REG's acquire a typical form in patients with cerebral atherosclerosis (Chapter 5). With development of the sclerotic process, the first positive wave becomes sharper and asymmetrical with regard to both its arms. A particularly obvious change in configuration of the curves consists of disappearance of the first negative wave and elevation thereof above the isoelectric line. In the presence of marked atherosclerosis there is a smooth, S-shaped transition from the first positive to the second negative wave.

The described changes are indicative of increased tonus of cerebral vessels, decrease and loss of elasticity of the vascular wall as a result of organic changes therein, which is also typical of the sclerotic stage of essential hypertension.

In the presence of essential hypertension (Chapter 6), grade I, unlike the curve with atherosclerosis, the first negative wave is almost always quite distinct. At the early sclerotic stage of this disease, the descending arm of the first positive wave forms a minimum above the isoelectric line, instead of the smooth S-shaped transition. This is a typical sign of arterial hypertension.

In the presence of arterial hypotension (Chapter 7), the velocity REG may be normal, but most often there are signs of increased resistance of cerebral vessels. In some cases, the increase in vascular tonus is more marked in the vertebrobasilar system, particularly in patients 40-60 years of age; in the opinion of the authors this is due to cervical osteochondrosis. As we see, in spite of low arterial pressure, regional craniocerebral hypertension was typical in patients with arterial hypotension. The authors observed relatively less often a decrease in tonus of cerebral vessels characterized by a high first positive wave, with extension of the descending arm, and lower location of the first negative wave than the second.

The changes in the velocity REG of patients with acute cerebrocirculatory disturbances (Chapter 9) are not specific for different forms thereof.

Very justifiably, the authors believe that modern clinical rheoencephalography should combine the possibility of both volumetric and velocity rheoencephalography. This expands significantly the diagnostic capabilities of the REG.

To sum up, it must be stressed that the book by V. Mitkov and P. Rashkov contains much valuable factual material. The theoretical generalizations and practical recommendations made on its basis are interesting and convincing.

This monography by Bulgarian authors will definitely be quite useful to both clinicians and physiologists, as well as pathophysiologists, dealing with cerebral circulation under normal and pathological conditions.

RULES FOR PREPARING ABSTRACTS OF ARTICLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 p 95

[Rules]

[Text] An abstract, no longer than two-thirds of a typewritten page must be enclosed with each original article sent to the editorial office, for translation into English. It should contain in brief the main content of the article. Emphasis should be laid on new information submitted in the article.

The abstract must inform foreign readers about the main points in the article and what it contains that is new, without having to refer to the text of the article. The use of generalities is not allowed.

The abstract should be prepared as follows:

Topic, object(s), nature and purpose of the work (wtihout repeating the title of the article).

Methods used (in cases where they are new or necessary to comprehend the substance and distinctions of the article).

Main theoretical and experimental results of the work. Preference should be given to new and tested facts, results of long-term studies that are important to the solution of practical problems. Indication must be made of whether the submitted digital data are primary or derived, the results of one or a series of observations; the range of accuracy, reliability and confidence intervals must be given.

Conclusions, evaluations, recommendations, adopted or rejected hypotheses discussed in the article.

Area of possible application of the results of the study.

The abstract should be as brief, precise and comprehensible as possible. The text of the abstract must not repeat the title of the article.

One should use standard terminology, or else explain the meaning of a term when it is first used.

Surnames should be given in their original transcription, with the exception of well-known names.

PUBLICATION OF NEW JOURNAL, 'IMMUNOLOGY,' ANNOUNCED

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 verso of front cover

[Announcement]

[Text] Attention specialists! Meditsina Publishing House has started publication in 1980 of the journal IMMUNOLOGIYA [Immunology], an organ of the USSR Academy of Medical Sciences.

This journal sheds light on the main theoretical and practical problems of general and applied immunology and allergology. It publishes the results of original research in the field of immunogenetics, molecular and cellular immunology, immunochemistry, biochemistry of immunogenesis, immunomorphology, functional bases of immunity, immunology of allergic reactions, clinical immunology and immunopathology.

The journal publishes articles on new methods of immunological and immunochemical analysis, which are recommended for clinical and experimental use, as well as brief reports containing basically new data on clinical and experimental immunology and allergology.

In this journal are published surveys dealing with the most pressing problems of general and applied immunology, allergology, congenital and acquired immunological disturbances, book reviews, information about scientific congresses and conferences, about the most important jubilee and anniversary dates.

It is intended for immunologists and allergologists, specialists in allied branches of medicine (biochemists, pathophysiologists, geneticists, hematologists, cytologists, etc.) and physicians concerned with problems of immunology, allergology and the use of immunological methods of examination in clinical practice.

It is published six times a year; subscription price is 7.80 rubles per year. It is sold by subscription only. Index 70421.

L-ASPARAGINASE AVAILABLE TO PHYSICIANS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1980 recto and verso of back cover

[Announcement by All-Union Information Office, USSR Ministry of Health]

[Text] L-Asparaginase (L-Asparaginasum) (lyophilized powder in 10,000 IU [international units] vials; price: 12.66 rubles); synonyms: krasnitin, leynase.

L-asparaginase is an enzyme product with antileukemic activity, the antineoplastic action of which is related to its influence on asparagine-dependent leukemic cells. This product has little influence on normal hemopoiesis; it reduces significantly the number of blast cells both in peripheral blood and bone marrow.

L-asparaginase is used by itself or in combination with other drugs for acute lymphoblastic leukemia, lymphosarcoma and reticulosarcoma.

A test is made of individual tolerance before instituting L-asparaginase therapy. For this purpose, 0.1 mℓ solution containing 10 IU L-asparaginase, is injected intracutaneously in the lateral aspect of the arm. Concurrently, as a control, the same amount of isotonic sodium chloride is injected next to the first injection. The reaction is evaluated after 3 h. If the diameter of the papule does not exceed 1 cm the test is considered negative, and one can commence treatment with L-asparaginase.

L-asparaginase is also given intravenously, by injection or drip infusion. The single dosage of the product is dissolved in 20-40 mℓ isotonic sodium chloride solution and given slowly for injections.

For drip infusion, the single dose is dissolved in 150 mℓ isotonic sodium chloride and infused for 30-40 min.

The single dose for adults and children is 200-300 IU/kg. A course consists of 300,000-400,000 IU for adults. The dosage for the course for children is reduced in accordance with their weight. Duration of the course is 3 weeks.

This product is prescribed for all forms of acute leukemia and generalized forms of hematosarcoma with blastosis in peripheral blood and bone marrow, regardless of peripheral blood parameters. In other cases, treatment is started when there are at least 3000/mm^3 leukocytes and 100,000/mm^3 thrombocytes in peripheral blood.

To evaluate the effect of this product in the presence of blasts in peripheral blood, a bone marrow punctate is examined before and after the course of therapy. The size of tumors is measured in cases of hematosarcoma.

One may observe nausea, vomiting, temperature elevation with chills and eruptions during administration of L-asparaginase. These complications usually disappear with the use of symptomatic agents (antipyretics, calcium chloride, antihistamines), and they do not serve as a contraindication to continued treatment.

There may be functional impairment of the liver and pancreas during administration of L-asparaginase; for this reason, it is imperative to constantly monitor (at least once a week) blood bilirubin, cholesterol, total protein, protein fractions, transaminase, alkaline phosphatase, diastase, etc., during the course of therapy. In case of appearance of severe and progressive changes in the above parameters, treatment must be stopped and symptomatic therapy prescribed.

Treatment with L-asparaginase may be associated with changes in the blood clotting system. With prothrombin level below 60% and fibrinogen concentration of less than 300 mg%, with concurrent increase in bleeding time, administration of this product should be stopped and appropriate treatment instituted.

L-asparaginase is contraindicated in the presence of pregnancy, diseases of the liver, kidneys, pancreas and central nervous system, with functional impairment of these systems.

It is on list B. It should be stored at temperatures not exceeding +10°C. This product is dispensed by prescription in pharmacies.

[007-10,657]

10,657
CSO: 1849 END

END OF FICHE DATE FILMED

Sept. 25, 1980